# HOMOLYTIC DISPLACEMENTS AT SATURATED CARBON CENTRE AND MOLECULAR INSERTIONS INTO Co-C BOND IN ORGANOCOBALOXIMES

*A Thesis Presented*

*by*

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*Dedicated*

*To*

*My Parents*

## STATEMENT

I hereby declare that the matter embodied in this thesis, 'Homolytic Displacements at Saturated Carbon Centre and Molecular Insertions into Co-C Bond in Organocobaloximes' is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology, Kanpur, India, under the supervision of Professor B.D. Gupta.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigations. The author is responsible for purely unintentional oversights and errors which could be traced herein.

MAHESWAR ROY

Kanpur:
May 1988

# CERTIFICATE

Certified that the work 'Homolytic Displacements at Saturated Carbon Centre and Molecular Insertions into Co–C Bond in Organocobaloximes' presented in this thesis, has been carried out by Mr. Maheswar Roy under my supervision and the same has not been submitted elsewhere for a degree.

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## CERTIFICATE OF COURSE WORK

This is to certify that Mr. Maheswar Roy has satisfactorily completed all the course requirements for Ph.D. degree programme in chemistry. The courses include:

Chm 505 Principles of Organic Chemistry

Chm 524 Modern Physical Methods in Chemistry

Chm 525 Principles of Physical Chemistry

Chm 542 Advanced Inorganic Chemistry II

Chm 545 Principles of Inorganic Chemistry

Chm 646 Bioinorganic Chemistry

Chm 800 General Seminar

Chm 801 Graduate Seminar

Chm 900 Post Graduate Research

Mr. Maheswar Roy has successfully completed his Ph.D. written and oral qualifying examinations and was admitted to the candidacy of the Ph.D. degree January 1985.

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## SYNOPSIS

The past two decades has seen a great deal of work on the organocobalt complexes and particularly on the organocobaloximes and the study has virtually opened up a novel area in organometallic reactions which orginates from the homolytic and heterolytic cleavage of Co–C $\sigma$ bond. Its potential as model for vitamin $B_{12}$ coenzyme is widely accepted and the study of such complexes in unfolding the mechanism of $B_{12}$ dependent reactions, if not overwhelming, but has been vital enough to focus at the initial stages of the $B_{12}$ catalytic cycle. Recently, these complexes have shown a remarkable ability as precursors for the synthesis of organic moieties.

The thesis entitled ''Homolytic Displacements at Saturated Carbon Centre and Molecular Insertions into Co–C Bond in Organocobaloximes'' deals with the organometallic aspects of organocobaloxime chemistry. The work has been divided into three chapters.

In the first chapter, a comprehensive and uptodate account of the literature on organocobaloximes has been covered. The particular emphasis has been given on the issues like Co–C bond stability, potentiality as synthetic organic precursor and model for coenzyme $B_{12}$.

The use of transition metal complexes in organic synthesis has seen considerable development in the past ten years or so. In these reactions, which can be stoichiometric or catalytic, the organic substrates are often employed as π ligands which undergo electrophilic or nucleophilic attack by various reagents. Radical reactions of synthetic utility using transition metal complexes are by contrast scarce. One amongst such radical reactions is the homolytic displacement reaction at saturated carbon generally referred to $S_H2$ reactions. These however, have rarely been discussed in literature and often described as highly improbable reactions. We have very successfully employed organo-cobaloximes for such a study and the work has been described in the 2nd chapter of the thesis. The 2nd chapter has two parts. In the first part, the reactions of benzyl cobaloximes, $4R\text{-}C_6H_4\text{-}CH_2Co^{III}(dmgH)_2Py$, (R = H, Me, Cl, Br, CN, $NO_2$) and heteroaromatic methyl cobaloximes, $RCo^{III}(dmgH)_2Py$ (R = 2 and 3 thienylmethyl, furfuryl and 3 furylmethyl) with benzene sulphonyl chlorides and substituted benzene sulphonyl chlorides (4-methyl, 4-methoxy, 4-chloro, 4-bromo and 2,4,5-trichloro) are described. The reactions are carried out under anaerobic and photochemical conditions (irradiation by 2 x 200 watt tungsten lamps). In case of benzyl cobaloximes, a mixture of products including benzyl sulphones, bibenzyls and benzyl ethers of dimethylglyoxime are obtained in varying proportions depending upon the substrate

cobaloximes and the nature of benzene sulphonyl chloride. The yield of sulphone is increased by $\approx 20\%$, with the concommitant decrease in bibenzyl and no formation of benzyl ethers of dimethylglyoxime, when the same reactions are carried out in the presence of 1-2 mol excess of pyridine. On the other hand, the corresponding reactions of heteroaromatic methyl cobaloximes with benzene sulphonyl chlorides with or without the presence of excess pyridine, form exclusively the corresponding sulphones in very good yield.

All the reactions described are free radical in nature. The reactions are believed to take place through a chain mechanism in which cobaloxime(II), present adventitiously or formed by partial homolysis of the substrate cobaloxime, abstracts a chlorine atom from the organosulphonyl chloride to give the organosulphonyl radical $R\dot{S}O_2$, which then attacks the $\alpha$ carbon of the organocobaloxime. Thereby, it displaces cobaloxime(II) and the desired sulphone is formed. A mechanism for the formation of bibenzyls and benzyl ethers of dimethylglyoxime has also been given. We believe that these products are formed by an attack of the $R\dot{S}O_2$ radical on the intermediate penta coordinate organocobaloxime.

In the second part of this chapter, an attempt has been made to study $S_H2$ reactions with the carbon centred radicals. As Mn(III) acetate has been shown to be a good source for the $\dot{C}H_2COOH$ radicals at $150^{\circ}C$, we have carried out its reactions with a variety of benzyl and heteroaromaticmethyl cobaloximes. In all the

reactions studied, no formation of substituted acetic acid is observed, however organoethers of dimethylglyoxime are the exclusive organic products formed in good yield. The same products are formed even when the reactions are done at lower temperatures like, 90°, 60° and 40°C. The products point to the facile one electron oxidation of organocobalt(III) to organocobalt(IV). The participation of organocobalt(IV) is novel. The formation of the monoethers has been explained by an intramolecular decomposition of the intermediate organocobalt(IV) species.

Insertion of small molecules into M–C σ bond continues to be a thrust area in organometallic chemistry. The area is of utmost importance particularly in organocobalt chemistry because of the yet incomplete understanding of the structure vs Co–C bond reactivity relationship in coenzyme $B_{12}$ and its model compounds. The third chapter of the thesis deals with the molecular insertions of oxygen and sulphur dioxide into Co–C bond in organocobaloximes.

Both $SO_2$ and $O_2$ insertions into Co–C bond are carried out with organocobaloximes, $RCo^{III}(L_2)Py$ under photochemical conditions (irradiation by 2 x 200 watt tungsten lamps) at 0° to −10°C.

$$RCo^{III}(L_2)Py \;)\; XY \xrightarrow[0-(-10^{\circ}C)]{h\nu} R(XY)Co^{III}(L_2)Py$$

$$XY = SO_2 \text{ or } O_2$$

R = Benzyl and substituted benzyl, heteroaromaticmethyl

L = dmgH (dimethylglyoxime monoanion)

or ChgH (cyclohexane glyoxime monoanion)

No insertion is observed under thermal conditions (refluxing dichloromethane) in dark. The reactions show all the characteristics of free radical nature.

In case of $SO_2$ insertions, s-sulphinato inserted products are formed as exclusive organometallic products. We believe from the experimental observations that these are not true insertions and the products result as an artefact of free radical chain process. The view point has been supported by independent experiments, for example, when an equimolar mixture of two organocobaloximes is reacted with sulphur dioxide gas, besides the expected products, two additional inserted products are formed as a result of cross insertion. These products can arise only if the chain process is operative.

Oxygen insertions, on the other hand, are non chain free radical processes. The detailed kinetic study has been done on these insertions by changing i) the axial base ligand, ii) equatorial ligand and iii) the axial organic group R. Based on the kinetic data, a radical cage mechanism has been proposed.

The $^1H$ NMR spectra of heteroaromaticmethyl cobaloximes and their inserted products show an unexpected 1:3 non-equivalence of the methyl groups on the equatorial dimethylglyoximato ligands. This has been attributed to the hydrogen bond formation between the oxime hydrogen and the heteroatom of the axial organic group.

Finally, a summary of the main results of work and scope for the future investigations is presented.

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6. Sulphur dioxide Insertions into organocobaloximes,
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   (Manuscript under preparation).

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Maheswar Roy

CONTENTS



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# CHAPTER - 1

## ORGANOCOBALOXIMES: A VERSATILE SYSTEM:

Transition metal-carbon σ bonded organometallics, Potential synthetic organic precursor and Catalyst, Model for $B_{12}$.

### Introduction

Organometallic compounds are the organic compounds, containing direct metal-carbon bonds. Their chemistry is the border area between the classical subdivision of organic and inorganic chemistry. Organometallic chemistry thus covers:

a) the compounds in which metal and carbon are linked by σ bonds;

b) metal carbonyls and their derivatives and

c) compounds in which unsaturated organic molecules are bonded to metals through π-bonds.

The organometallic chemistry advents back to 18th century when tetramethyldiarsine was obtained as a byproduct in the photolysis of cobalt ore smaltite.[1] It took almost one hundred years to characterise the compound.[2] Frankland in 1849 isolated and

characterised diethylzinc – the first ever organometallic compound with metal to ligand σ bond.[3] On the other hand, the first olefin-metal compound, the Zeise's salt was reported in 1827.[4,5]

Since then a tremendous effort has been made by scientists to synthesize and study a large number of organometallic compounds. The names of Grignard, Gilman, Zeigler, Wilkinson and many others are very significant in this century for their contribution to organometallic chemistry. Their work has been very well documented and reviewed in literature.[6-15]

## 1.1 Organocobalt Complex: Dormant Phase

Upto the middle of this century, the field of organo-cobalt chemistry was limited to a group of ill-defined alkyl and aryl-compounds.[16] However, with the great expansion of organometallic chemistry in the late 1950's and aided by the knowledge that carbon to transition metal bond might be stabilized by certain ligands, there was also some progress into the preparation of compounds containing Co-C bond.[17] Dialkyl cobalt, used commercially as an additive in drying oils, may be considered as the first stable complex of cobalt.[18] Complexes of empirical formula $RCoX_n$ (R = α- or β- thyl; X = Br, I) have been prepared but partially characterized by Ingles and Polya.[19] Besides, a few acetylide complexes,[20] aryl complexes,[21] partially or fully characterized, and isolated in very poor yields, have also been reported in literature.[22,23]

Though by late fifties it became clear that the σ bonded organometallic compounds of the main group elements and transition metals contribute a diverse and rich field of research. However, organo-cobalt chemistry especially that of Co-C sigma bond could not be established to a similar extent even by the middle of this century.

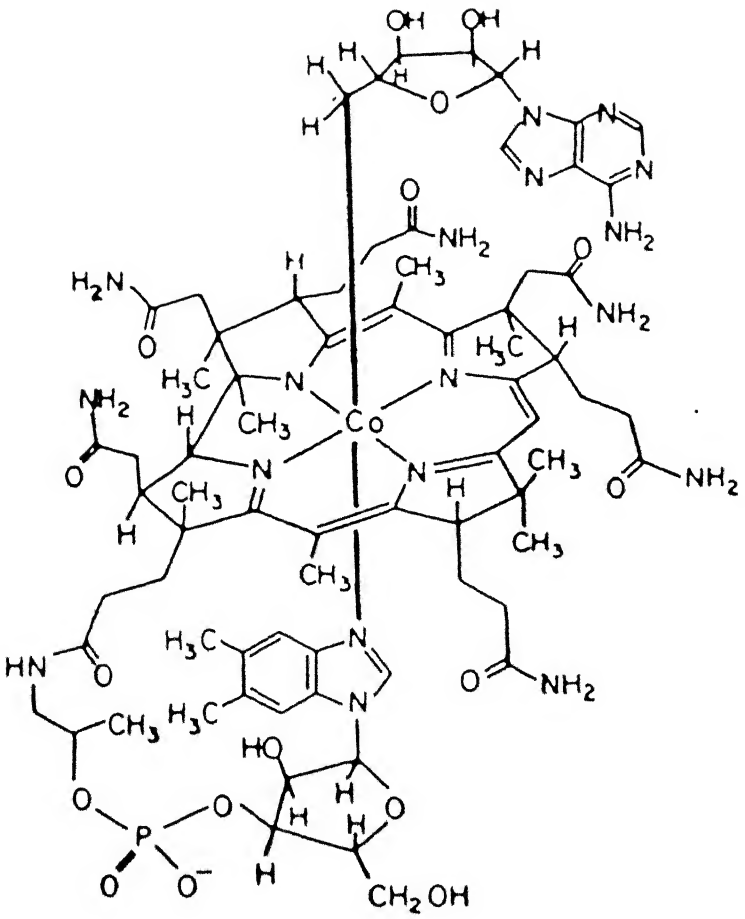
## 1.2 Co-C bond: A new era

In 1962, in a brilliant X-ray crystallographic study by Dorothy Hodgkin and Galen Lenhert established that the naturally occuring molecule, vitamin $B_{12}$ coenzyme, contained a cobalt carbon bond.[24] It was for the first time that a naturally occurring transition metal organometallic compound was recognized and was one of the most stable sigma bonded organo-cobalt compound ever reported. The contemporary chemical studies showed that this bond was unaffected by a number of reagents which cleaved bonds elsewhere in the molecule.[25] The structure of vitamin $B_{12}$ coenzyme (Fig. 1) points out the following salient features:

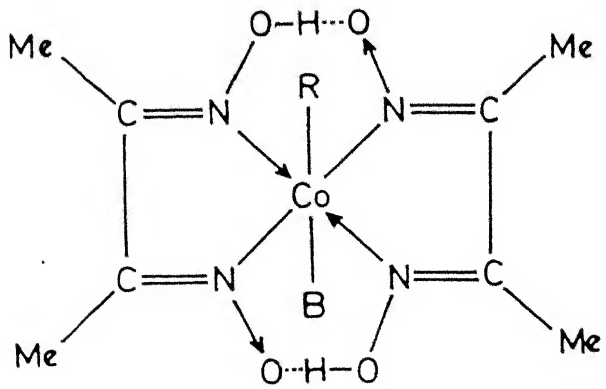
a) an axial Co-C σ bond between cobalt and the ribosyl portion of Adenosyl group,

b) an equatorial ring structure comprising of four donor nitrogen atoms from pyrrole groups of the macrocyclic corrin ring,

c) an axial base ligand, normally a derivative of benzimidazole.



Coenzyme $B_{12}$



Organocobaloxime

Fig. 1 Reproduced from ref.[109]

The above features are common to all vitamin $B_{12}$ derivatives, but with changes in axial ligands bound to cobalt. In general, all molecules exhibiting the tetrapyrrole corrin ring structure are referred to as corrinoids. When the base ligand is an α-5,6-dimethylbenzimidazole nucleotide as in Fig. 1, the molecule is termed as cobalamin. Although majority of the $B_{12}$ derivatives are diamagnetic (disregarding a small amount of temperature independent paramagnetism) with cobalt in +3 oxidation state, other lower oxidation states of cobalt also exist. The derivatives with +1 and +2 states are referred to as Cob(I)alamin and Cob(II)alamin respectively.

The realisation of the fact that vitamin $B_{12}$ coenzyme, formally a complex of cobalt (III), and the corrin ring might be an important factor in the stabilization of Co–C bond, led to a wide consideration of the possibility that other carbon-cobalt(III) compounds might be formed with the same or analogous ligands. These ideas[26,27] led the synthetic inorganic chemists to the synthesis of a large number of σ bonded organocobalt complexes.

## 1.3 Co–C σ Bond: Synthesis Begins . . .

The problems faced by chemists in synthesizing stable compounds with Co–C bond started fading away in early sixties following studies related to cobalamin derivatives.[28] Many cobalamin derivatives were prepared. The progress in organocobalamins stimulated interest in the preparation and study of

other organocobalt complexes and the year 1964 may be designated as a landmark in this field with the name of G.N. Schrauzer who reported a number of organobis(dimethylglyoximato)cobalt complexes, later known as cobaloximes.[29] It was soon established that the stability of Co-C bond virtually depended upon significantly and optimally strong, essentially planar ligand field. Moreover, the coordinating atom need not be nitrogen every time. Today a wide variety of such equatorial ligand systems are known that ranges from aromatic porphyrins[30] to the completely saturated [14]-ane $N_4$ systems[31] with more than two thousand and five hundred organocobalt complexes in the literature. The driving force behind these works has been the attempt to elucidate the mechanism of the $B_{12}$-dependent enzymatic reactions by studying the reactions of model compounds. However, it must be emphasized that because of their close similarity of chemical properties to vitamin $B_{12}$ coenzyme, cobaloximes were the most studied ones.[32]

### 1.3.1 General Methods of Synthesis of Organocobalt Complexes

The preparation of organocobalt complexes has offered interesting and useful reactions in organometallic chemistry. These complexes have been prepared by a large number of ways and have enriched the organometallic chemistry and paved way for the synthesis of various other organometallic compounds.

Many reviews have explored the preparative methods.[33-40]

The general methods of preparation are broadly classified into the following main categories (Table 1.1).

A. Reaction of ($Co^{I}$) or Co-hydride species with electrophilic reagents.

B. Reaction of ($Co^{II}$) reagents with free radicals.

C. Reaction of ($Co^{III}$) complexes with nucleophiles.

D. Modification of an organocobalt complex.

## A.1 From ($Co^{I}$) Complexes

This method has exploited the high nucleophilic reactivity of $Co^{I}$ species[41] which has been called as supernucleophiles by G.N. Scrauzer.[41a] The Pearson nucleophilicity of ($Co^{I}$) derived from cobalamin and its model compounds, lie within the range $14.0 \pm 0.5$ which is many fold higher than those of conventional nucleophiles like $CN^{-}$ (6.70) and $I^{-}$ (7.42).[41a] Among all the methods known so far, this is the best method, which involves the attack of a ($Co^{I}$) species at the electrophilic centre of an alkylating reagent (RX)[33]

$$(Co^{I}) + RX \longrightarrow (Co^{III})\text{-}R + X^{-}$$

where R may be alkyl, allyl, benzyl, acyl, alkenyl, alkynyl etc. while $X^{-}$ may be $Cl^{-}$, $Br^{-}$, $I^{-}$, tosylate and less commonly carboxylate, sulphate, phosphate, anhydride, trimethylamine and even mercury metal or nitrogen of diazomethane.

Table 1.1. Summary of Methods of Preparation of Organocobalt(III) Complexes

| Section | Inorganic reagent | Organic substrate | Products |
|---|---|---|---|
| A.1 | $(Co^{I})$ | RX; X = halide, tosylate etc. | $R(Co^{III}) + X^{-}$ |
| | $(Co^{I})$ | $R\overline{CHCH_2X}$ ; X = O, NH etc. | $RCHOHCH_2(Co^{III})$ |
| | $(Co^{I})$ | XCH=CHPh; X = Br, Cl | $PhCH{=}CH(Co^{III}) + X^{-}$ |
| | $(Co^{I})$ | $XCH{=}CH_2$; X = CN etc. | $XCH_2CH_2(Co^{III})$ |
| | $(Co^{I})$ | XC≡CH; X = Ph etc. | $XCH{=}CH(Co^{III})$ |
| A.2 | $H(Co^{III})$ | $RCH{=}CH_2$ | $MeCHR(Co^{III})$ |
| | $H(Co^{III})$ | RC≡CH | $CH_2{=}CR(Co^{III})$ |
| | $H(Co^{III})$ | $PhNH_2/HCHO$ | $pHNHCH_2(Co^{III}) + H_2O$ |
| B. | $(Co^{II})$ | RX; X = halide | $R(Co^{III}) + X(Co^{III})$ |
| | $(Co^{II})$ | $RNHNH_2/O_2$ | $R(Co^{III}) + N_2 + H_2O$ |
| | $(Co^{II})$ | $RCMe_2OOH$ | $R(Co^{III}) + OH(Co^{III}) + Me_2CO$ |
| C. | $X(Co^{III})$; H = halide | RM; M = metal | $R(Co^{III}) + MX$ |
| | $X(Co^{III})$; X = halide | $CH_2{=}CHOR/ROH$ | $(RO)_2CHCH_2(Co^{III})$ |
| | $RO(Co^{III})$ | $R^1CH_3$; $R^1$ = CN etc. | $R^1CH_2(Co^{III}) + ROH$ |
| D. | $RO_2CCH_2(Co^{III})$ + $OH^-/H^+$ | - | $HO_2CCH_2(Co^{III})$ |
| | $HOCH_2CH_2(Co^{III})$ + $Ac_2O/ROH/RCO_2H$ | - | $XOCH_2CH_2(Co^{III})$; X = Ac, R, $CO_2R$ |

Cobalt(I) species are generated by,

i) reduction of ($Co^{II}$) or ($Co^{III}$) reagents by sodium borohydride in alkaline medium,

ii) disproportionation of ($Co^{II}$) to ($Co^{III}$) and ($Co^{I}$) in highly alkaline medium, and

iii) reduction of ($Co^{II}$) by hydrogen in acidic, neutral as well as in alkaline medium.

Reduction of ($Co^{III}$) chelates other than cobaloximes is done by sodium, potassium metals or their amalgams. For cobaloximes, method (i) and (ii) mentioned above, are employed most. However, for the base sensitive alkylating agents method (iii) is found to be most effective. The reduction is generally carried out at temperatures below $0^{o}C$ under inert atmosphere of nitrogen or argon and is visibly sharp - a brown ($Co^{II}$) complex changing over to green to blue ($Co^{I}$) species. The mechanism of ($Co^{I}$) substitution of alkylhalides and tosylates is not certain as was once beleived, evidence has been presented in support of $S_N2$ as well as an electron transfer mechanism.[39] The main lines of evidence for an $S_N2$ process come from rate analogies and stereochemical studies. Some stereochemical studies involving $Co^{I}(dmgH)_2Py$ and saturated alkyl halides, tosylates and epoxides have demonstrated inversion of configuration at the substituted carbon.[42-44]

An electron-transfer mechanism has recently been proposed in a number of cases.[45-49] Thus, the reaction of ($Co^{I}$) with different isomers of sterically hindered bromides (1, 3, 4) reveal

$$S_N2 \quad : (Co^{I}) + R\text{-}X \longrightarrow R(Co^{III}) + X^{-}$$

Electron transfer:

$$Co^{I} + RX \longrightarrow (Co^{II}) + \dot{R}\dot{X}$$

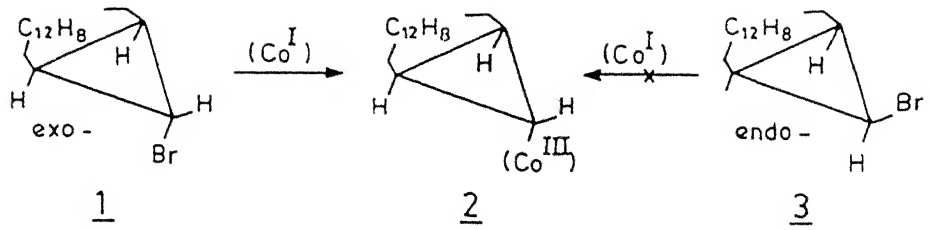
$$\dot{R}\dot{X} \longrightarrow R^{\bullet} + X^{-}$$

$$(Co^{II}) + R^{\bullet} \longrightarrow R(Co^{III})$$

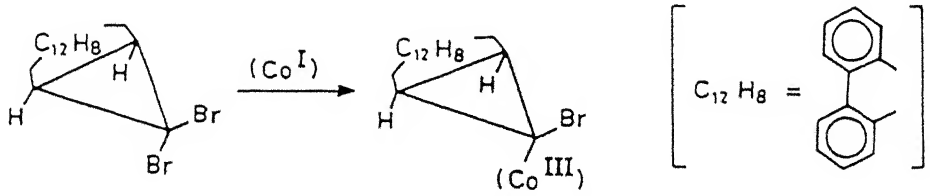
that only exo-structures, 1 and 4 yield the corresponding cobaloximes 2 and 5, while the endo-analogue 3 remains unreactive (Scheme 1.1).[45] An electron transfer mechanism has been proposed for these reactions, the retention being a consequence of shielding by the dihydrophenanthrene moiety. A retentive alkylation of ($Co^{I}$) has also been reported with the sterically hindered halides 6 to 8 (Scheme 1.1).[46]

A conclusive evidence for the electron transfer mechanism has recently been reported by Tada et al. in the reaction of 2-(allyloxy)ethylhalide with ($Co^{I}$).[49] The mechanism is outlined in (Scheme 1.2). 2-(Allyloxy)ethyl halide 9 having a substituent at β-position ($R^1 \neq H$) gives only the cyclized cobaloxime 10 via the electron transfer routes A, B, C and D. The corresponding reaction of 9 ($R^1 = R^2 = H$; X = tosylate) gives exclusively the direct substitution product 11 by an $S_N2$ mechanism (Route E).

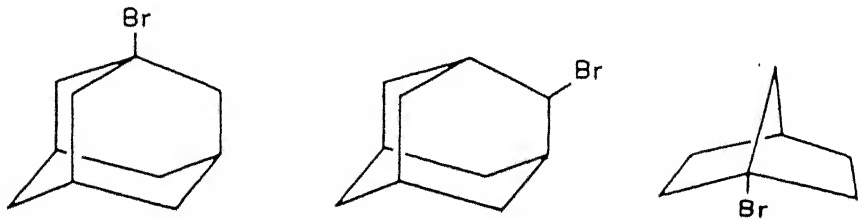
## Scheme 1.1




1 2 3

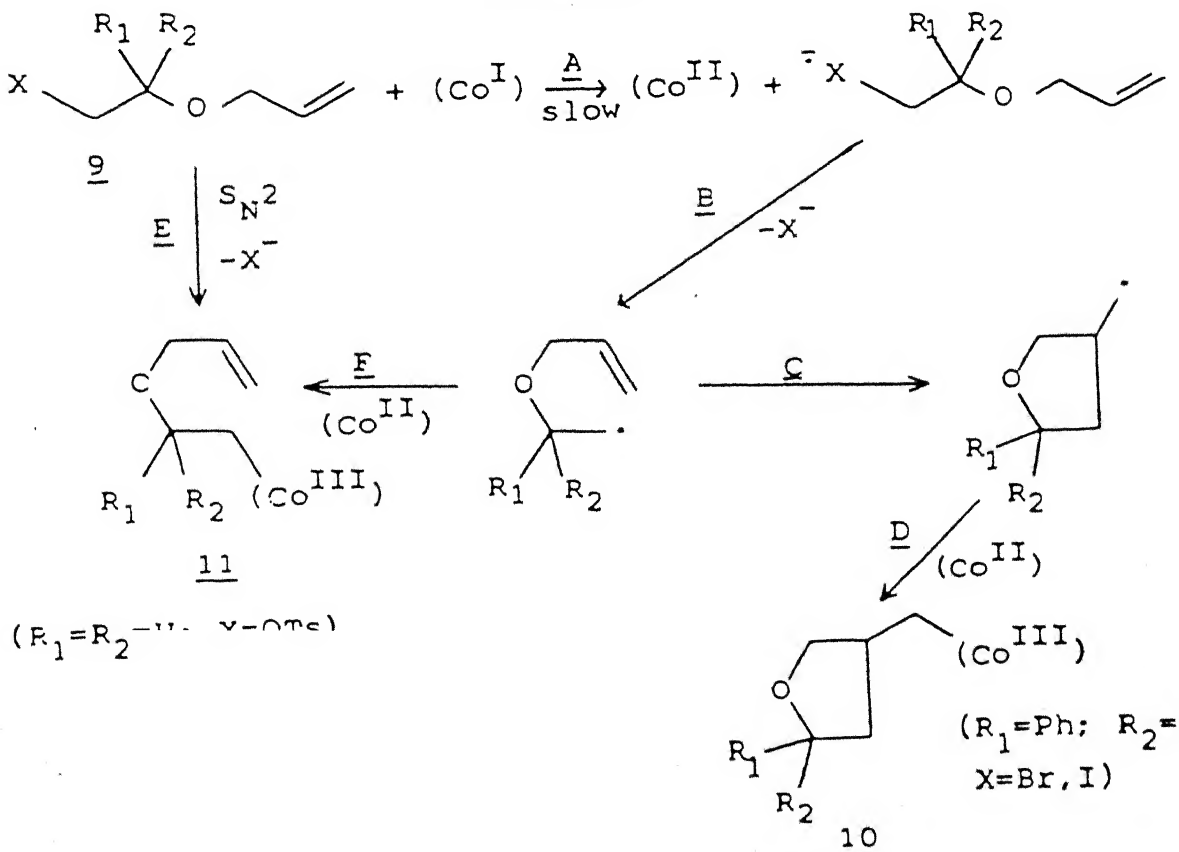



4 5



6 7 8

## SCHEME 1.2



However, the formation of a mixture of 10 and 11 from 9 ($R^1$ = $R^2$ = H; X = Br, I) suggests the operation of both the processes simultaneously and even a new route F where ($Co^{II}$) capture by the organic radical takes place.

Besides the substitution reaction, cobalt(I) reagents add to unsaturated electrophiles. For example, it rapidly reacts with acrylonitrile and other such activated alkenes to give π-complexes which then slowly rearrange to the β-substituted cobaloxime.[50]

$$(Co^{I}) + XCH{=}CH_2 \xrightarrow{\text{fast}} \begin{matrix} CHX \\ \| \\ CH_2 \end{matrix} \!\!-\!\!(Co^{I}) \xrightarrow{\text{slow}} XCH_2CH_2(Co^{III})$$

(X = CN, COOR)

Similar addition reactions have also been demonstrated with alkynes.[51-53] The mechanism involves nucleophilic attack by ($Co^{I}$) (syn-addition on the β carbon atom of alkyne, via a π complex, followed by rapid trans addition of a solvent proton:

$$(Co^{I}) + XC{\equiv}CH \xrightarrow{\text{slow}} \begin{matrix} X & & (Co^{III}) \\ & \diagdown\ \diagup & \\ & C{=}C & \\ & \diagup\ \diagdown & \\ & H & \end{matrix} \xrightarrow[\text{fast}]{\text{MeOH}} \begin{matrix} X & & (Co^{III}) \\ & \diagdown\ \diagup & \\ & C{=}C & \\ & \diagup\ \diagdown & \\ H & & H \end{matrix}$$

(X = Ph, $CO_2R$, $CH_2OH$, $CF_3$, $CH_2CO_2Me$)

However, with propargyl alcohol (X = $CH_2OH$) a mixture of α and β substituted products is obtained while propyne (X = $CH_3$) gives only the α-substituted product.

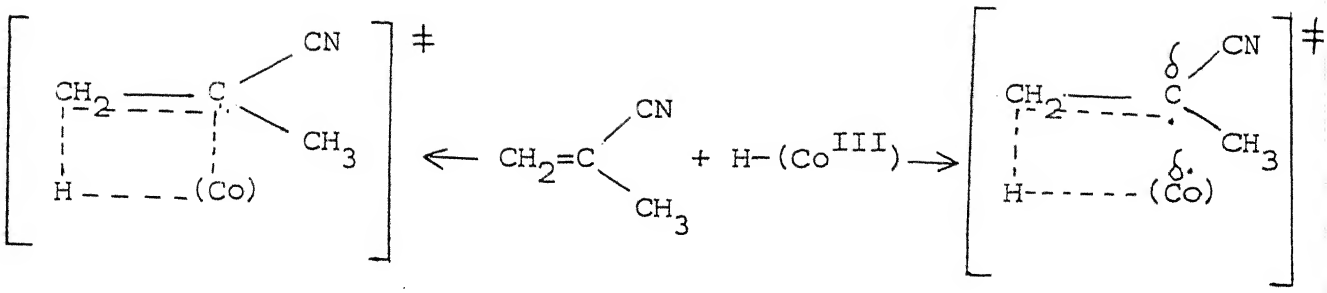
Recently, 2-aryl-2-hydroxyethyl, 2-alkoxyethyl, 2-hydroxyethyl, cobaloximes have been prepared using this method.[54-56] Synthesis of other novel cobaloximes have been achieved using the similar method.[57] Dialkylcobaloximes of the general formula $RCo(dmgH)_2NCCo(dmgH)_2B$ have also been reported in literature.[58]

A.2 From Cobalt Hydride Reagent

The ($Co^I$) complexes in less basic medium may reversibly pick-up a proton to give the corresponding cobalt(III) complex with a coordinated hydride:[59,60]

$$(Co^I) + H^+ \rightleftharpoons H\text{-}(Co^{III})$$

Being the conjugate acid of ($Co^I$) the hydrido complex decomposes in alkaline medium to ($Co^I$) thereby undergoing most of substitution reactions described for the latter[61] (Sec. 1.3.1/A.1). This reagent, however, has been exploited most for the synthesis of pentacyanocobalt(III) and cobalamin derivatives. Interestingly the addition of hydrido species across the double and triple bond produces α-substituted derivatives, unlike that of ($Co^I$) as discussed previously. Kinetic studies indicate the possibility of two different mechanisms, one with a four centred transition state (12) and the other with a biradical transition state (13), the former being a more favourable one:[50,62]



12 13

The stereochemical course has been investigated by Gaudemer et al.[50,63] The following example provides another interesting variation of the addition reaction of cobalt hydride.[64] The mechanism may involve the attack of the hydrido species on the carbinolamine formed *in situ* from aniline and formaldehyde:

$$H(Co^{III}) + PhNH_2 + HCHO \longrightarrow Ph\text{-}NHCH_2(Co^{III}) + H_2O$$

Monothiocarbamic S-esters have apparently not been described as ligands, however, reacting pyridinebis(dimethylglyoximato)-cobalt(II) under $H_2$ atmosphere with monothiocarbamic vinyl ester, yields corresponding organocobaloxime.[65]

$$Co^{II}(dmgH)_2Py + R_1R_2NC(O)S\text{-}CH{=}CH_2 + 1/2\ H_2$$

$$\xrightarrow[25^{\circ}C]{MeOH} R_1R_2NC(O)S\text{-}\underset{\displaystyle Co(dmgH)_2Py}{\underset{|}{CH}}\text{-}CH_3$$

$R_2$ = n-Pr; $R_1$ = Et, $R_2$ = n-Bu;
Et, $R_2$ = cyclohexyl).

B. Preparation from Cobalt(II) Complexes

Co(II) complexes are odd electron species as such and react with free radicals or via radical pathways. In general the overall net reaction for alkylation of $Co^{II}$ by RX is represented as

$$2L_5Co^{II} + RX \longrightarrow L_5Co^{III}R + L_5Co^{III}X$$

The method has a limited synthetic utility because of the cumbersome procedure to separate the two organocobalt species formed in equimolar quantities. However Widdowson and Roussi[66] have developed a method for cobaloxime preparation using Znwool to recycle halocobaloxime to Co(II) state until all Co(II) is converted to organocobalt(III) products.

Cobalt(II) complexes[67a] react with a number of organic and organometallic free radicals to form organocobalt(III) complexes. Alkylation of Co(II) complexes like Cob(II) alamin[67b] and several $B_{12}$ model compounds[60,68-71] by RX show second order kinetics with reaction rate versus $K[Co^{II}][RX]$. The reactivity of RX increases with increasing stability of the radical $R^{\bullet}$ (e.g., along the sequence $CH_2ClCOOR < CHCl_2COOR < CCl_3COOR$ and along the sequence R-Cl < R-Br < R-I. Halpern et al. have proved that these alkylation proceed by the following radical mechanism:[67,72,73]

$$[Co^{II}] + R\text{-}X \xrightarrow{\text{slow}} [Co^{III}\text{-}X] + R^{\bullet}$$

$$[Co^{II}] + R^{\bullet} \xrightarrow{\text{fast}} [Co^{III}\text{-}R]$$

Another interesting case is the reaction of tertiary alkylhydroperoxide ($RCMe_2OOH$) (R = Et, Ph etc.) with a number of ($Co^{II}$) chelates to form $R(Co^{III})$ complexes by the following mechanism:[74]

$$RCMe_2OOH + Co^{II} \xrightarrow{slow} RCMe_2O^{\bullet} + OH(Co^{III})$$

$$RCMe_2O^{\bullet} \xrightarrow{fast} R^{\bullet} + Me_2CO$$

$$\dot{R} + (Co^{II}) \longrightarrow R(Co^{III})$$

The synthesis of organocobalt(III) complexes from ($Co^{II}$) substrates has proved to be very useful in cases where

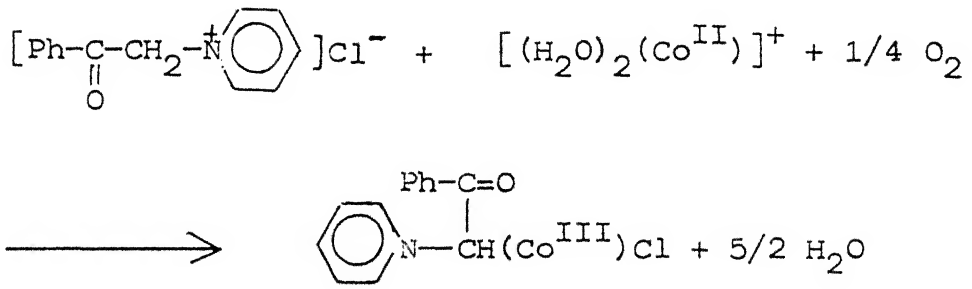
i) the generation of ($Co^{I}$) is difficult; for example, $[CoMe_6[14]\text{-ane } N_4]^+$, and

ii) the alkylating agent either is very susceptible to decomposition under reaction conditions or reacts very slowly with ($Co^{I}$) giving rise to poor yields or no yield of $R(Co^{III})$ at all, for example, many alkylcobaloximes have been synthesized by the reaction of ($Co^{II}$) with reactive halides such as α-halogeno esters in the presence of zinc wool in non-aqueous solvent.[66a]

Organic hydrazines have been shown to react with ($Co^{II}$) in the presence of molecular oxygen to form corresponding organocobalt(III) complexes:[75]

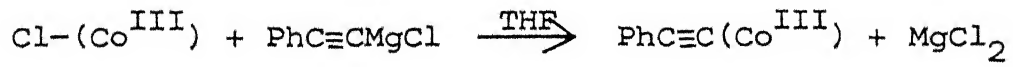
$$(Co^{II}) + RNHNH_2 \xrightarrow{O_2} R(Co^{III}) + N_2 \quad (R = H, Me, Ph)$$

An interesting example showing the use of ($Co^{II}$) reagents in the synthesis of ($RCo^{III}$) derivatives has recently been reported[76]



C. Preparation from Cobalt(III) Complexes

Reaction of ($Co^{III}$) complexes with nucleophilic carbon species is another method for the synthesis of organocobalt compounds. A number of stable halocobalt(III) complexes react with alkyl and aryl organolithium and organomagnesium reagents to form the corresponding organocobalt(III) complexes.[30,37,77-79]



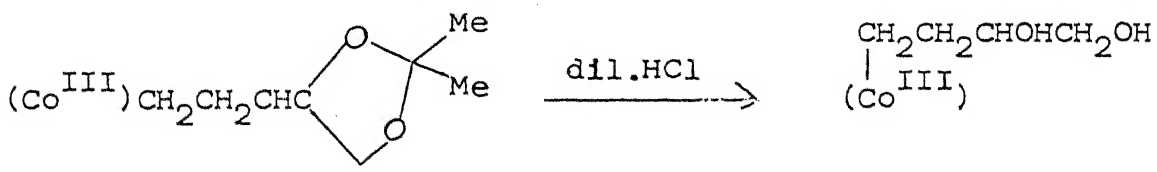
Poor solubility of halocobalt(III) complexes in ethereal solvents and the use of many-fold excess of Grignard's reagent are two main disadvantages of this method.

Neutral β-methylcobalamin (X = $CH_3$) is obtained from $B_{12a}$ (X = OH) with a new methylating agent ($(CH_3SiF_6)(NHCl)_3$).[80] In

D. Modification of Organic Ligands

Many organocobalt complexes that are difficult to prepare by the above conventional routes (A, B and C) have recently been synthesized by initially preparing a suitable chelate on which the axial or equatorial group functionalities are then modified, for example, solvolysis of ester functionality in axial organic ligand provides the simplest route to new cobaloximes.

Thus, meta- and para-substituted carboxyphenyl cobaloximes are synthesized in good yields by hydrolysis of corresponding methyl ester in 0.5 M KOH in aq. methanol.[88] Acetal hydrolysis of many cobaloximes and cobalamins also proceed smoothly in acidic medium:[89]




Hydroxy alkylcobaloximes have been used as precursors for many interesting transformations as illustrated below:[90]

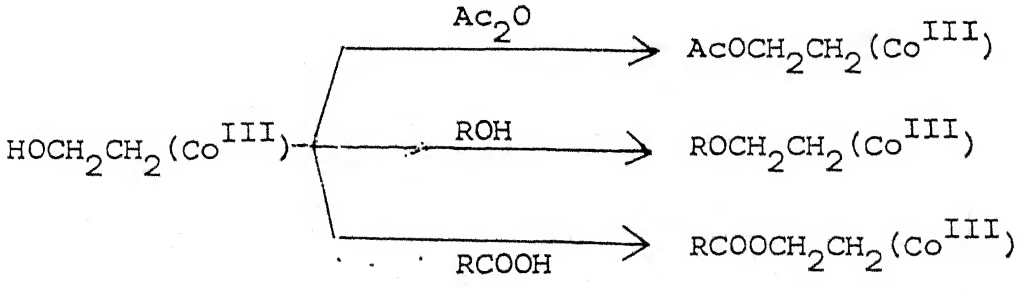
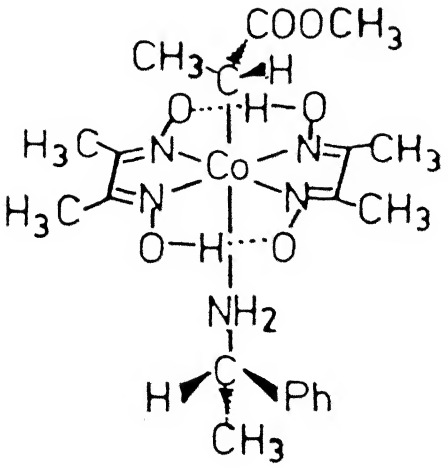


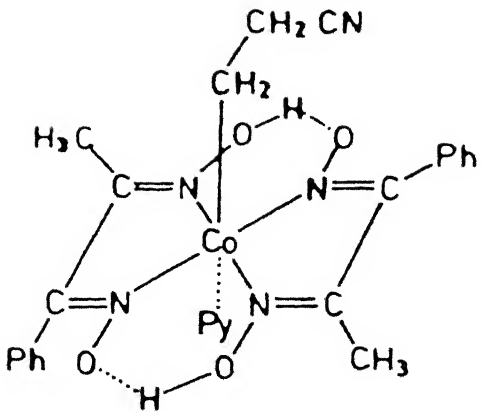
Table 1.2. The known examples of organocobaloximes with tertiary α-carbon atom

| R | Method of Synthesis |
|---|---|
| $Me_2CCN$ | A.1, A.2 |
| 1-Methyl-2,2-diphenyl-cyclopropyl | A.1 |
| t-Adamantyl | A.1 |
| t-Norbornyl | A.2 |
| $MeC(Me)CH{=}CH_2$ | A.1 |
| $MeC(Et)C{\equiv}CH$ | A.1 |
| $Me(OAc)(MeCOO)C$ | A.2 |
| $Cl_2CC(=O)OMe$ | B |
| $Cl_2CCN$ | B |
| $Cl_3C$ | B |
| $CMe_2COOMe$ | A |

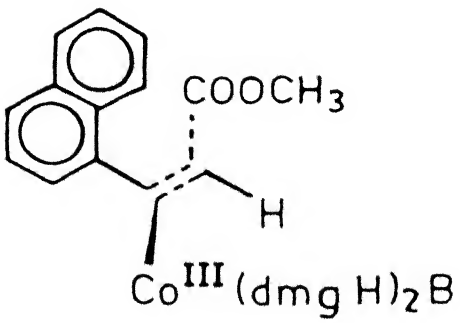
Since organocobaloximes have been used as catalysts in many reactions, a number of optically active cobaloximes have been synthesized with an aim that they will provide precise information about the elementary process of such catalytic reactions.[94-97] Representative examples are illustrated in Fig. 2 (14, 15). Besides, Gaudemer et al. have reported the first example of chiral atropisomeric cobaloxime (Fig. 2) (16)



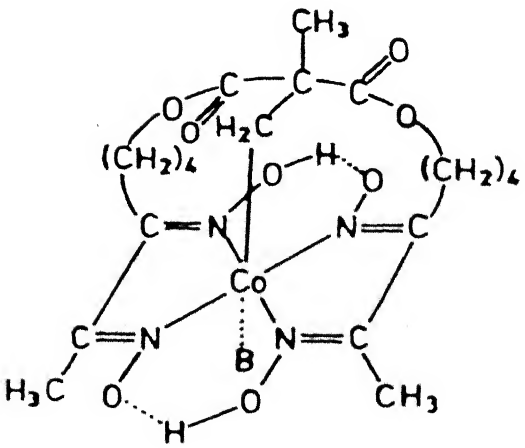

(14)




(15)




(16)




(17)

FIG. 2 NOVEL ORGANOCOBALOXIMES.

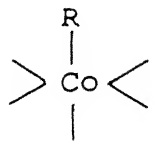
in which the rotation of the atropisomeric ligand is inhibited by the cobaloxime substituent.[98]

A number of novel intramolecularly bridged cobaloximes (Fig. 2, 17) have also been synthesized to model the $B_{12}$ dependent enzymatic methylmalonyl-Co mutase reaction.[99]

## 1.4 Cobaloximes: Physical Properties and Structures

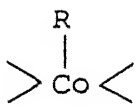
Though most organocobalt(III) complexes are unstable to visible light in solution, the solid complexes are stable to visible light. Secondary alkyl cobaloximes are less stable than primary alkylcobaloximes and there are very few examples of tertiary derivatives. All organocobalt(III) complexes for which magnetic susceptibilities have been determined are diamagnetic irrespective of their coordination.[35,100] X-ray structural studies have shown that organocobalt(III) complexes can exist in three different stereochemical configurations:

a) six coordinate, octahedral, orange in colour,
b) five coordinate, square pyramidal, green in colour, and
c) dimeric, consisting of two square pyramidal complexes, generally red in colour:



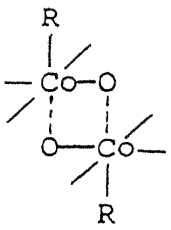
[a]

octahedral



[b]

square pyramidal



[c]

bridged octahedral

The four equatorial donor atom groups in all the complexes remain nearly planar but other parts of the chelate ring can exhibit large conformational changes as a consequence of the steric interactions with the axial ligands. Another interesting feature revealed by X-ray studies is the large Co-C-C bond angle observed when the coordinated carbon atom is tetrahedral. It has been suggested that the rehybridization is necessary in order to increase the overlap with the cobalt $\sigma$-metal orbital and to reduce repulsions between the non-bonded electron pairs on the cobalt and the electron pairs in the C-C and C-H bonds.[35] Furthermore, there appears to be a linear relationship between the Co-C bond length and the number of substituents on the carbon attached to cobalt. In general, it seems that in the organocobaloximes $[RCo(dmgH)_2B]$, steric interaction between bulky bases B and the equatorial ligand system, bend the equatorial ligand system towards axial organo ligand and provoke lengthening of the Co-C bond even by $> 0.1$ Å.[101,102]

In the organocobalt(III) complexes of the type $[RCo^{III}(L_4)B]$, the variation of Co–B bond distance is found when the organo group R is replaced by the inorganic ligands such as $Cl^-$, $NO_2^-$, or $CN^-$ and this has often been interpreted in terms of the strong trans-influence of the organo group. Indeed, both cis and trans influences have been noted in these complexes. When the equatorial ligand of an organocobaloxime lacks a plane of symmetry, isomers are possible. Similarly, organocobaloximes where R is optically active are also known.[33,35]

Approximate ab initio studies of geometrical deformation introduced in cobaloximes do not reveal the existence of any major electronic effects.[103] However, theoretical calculations[104,105] indicate that the metal atom of the cobalamin has a slightly smaller partial positive charge than that of cobaloxime, otherwise there is a close similarity in the nature of axial bonds involving the cobalt atom in both (Fig. 3).[106–108]

### 1.4.1 Electronic Spectra

In view of semiempirical calculation and EHMO theory, electronic structure of the cobaloxime has been considered and results of these calculations have been useful in the analysis of the electronic spectra. Three major bands appear for cobaloximes in general:

a) A band at 240 nm, assigned to $\pi$–$\pi^*$ transitions (in

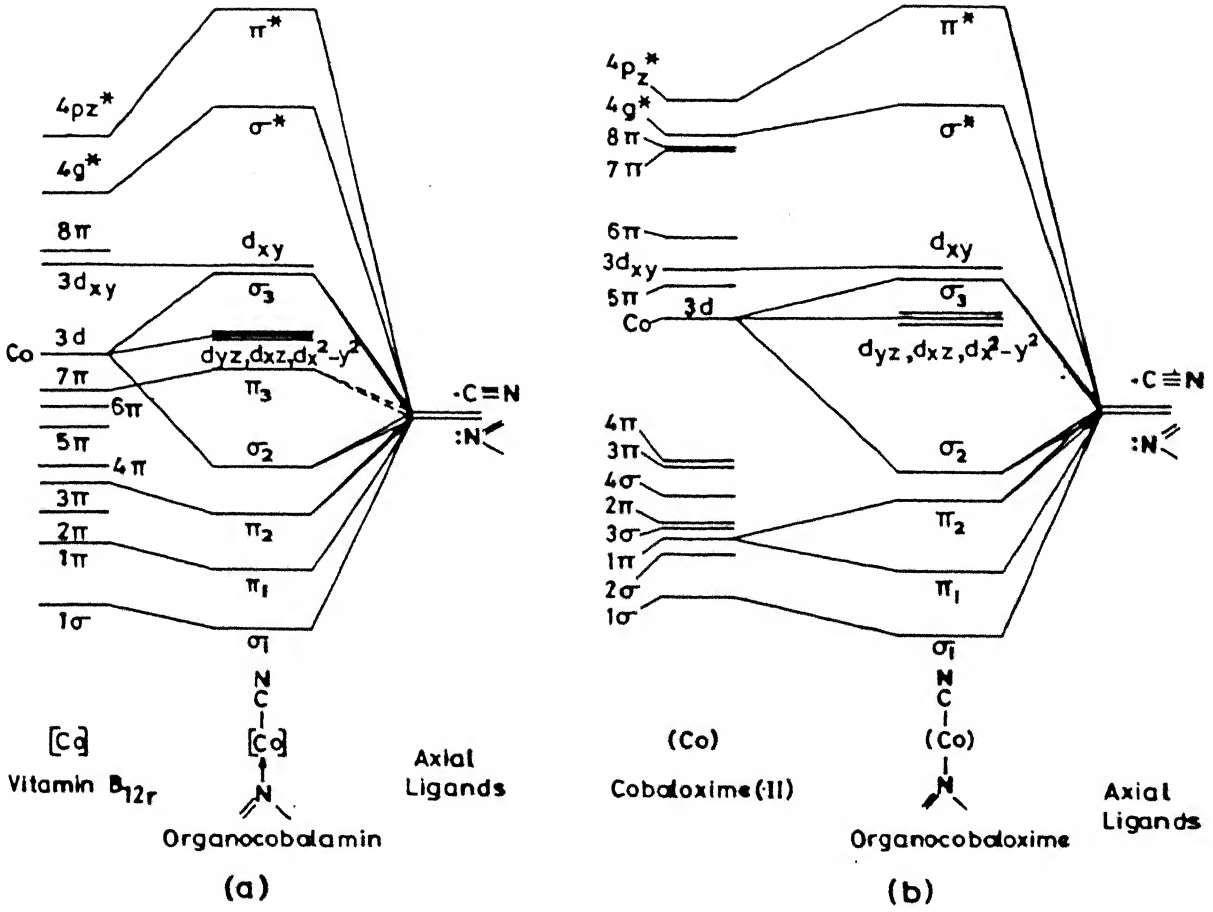



Fig. 3 Schematic M.O. diagram of Cobalamin and Cobaloxime showing the effect of axial ligands[106].

corrin system). However, this band appears at a higher wave length due to the extensive conjugation.

b) There are several but not well assigned bands between 400–250 nm. The axial bases may absorb in this region.

c) The important low energy absorption of the organocobaloxime occurs between 400–500 nm and is believed to be typical of the presence of covalent axial bonds in view of the $\varepsilon$ of about $10^3$. This band has been assigned to cobalt to carbon charge transfer band. Its energy depends on the axial base and also to some extent on the inductive effect and the partial 2s character of axial carbon residue attached to the cobalt atom.[109,110] This transition is shifted to higher energy on changing the hybridization of the carbon residue. Considering these arguments, the band can be assigned to $\sigma_2 - \sigma_3$,[106] but it has also been assigned to a $d-\pi^*$ transition[111] or d–d transition.[112,113] This band shifts to shorter wavelengths as the alkyl group becomes more electron withdrawing as well as when the donor ability of the axial base or equatorial ligand increases.

### 1.4.2 IR Spectra

The vibrational spectra of cobalamins and cobaloximes reflect very broad generalities. Thus, for any alkyl cobaloximes, the band at 1560 $cm^{-1}$ is attributed to C=N stretching frequency of dimethylglyoximato ligand and is dependent on the strength of the axial base ligand. The Co–C stretch appears in the far infrared region of the spectrum. The bands which may be used for partial characterization are $\nu_{OH----O}$ (1720–1760), $\nu_{N-O}$ (1230–1240 and 1080–1100) and $\nu_{C-N}$ (dmgH) (510–520) where

values in parentheses represent the approximated frequency region[114-117] (in $cm^{-1}$).

### 1.4.3 NMR Spectra

Because of diamagnetic nature of these complexes much information about their structure, intramolecular interaction and reactions, has come from the study of $^{1}H$ NMR,[40,118,119] $^{13}C$ NMR, $^{19}F$ NMR and $^{59}Co$-NMR spectroscopy.[120-123] $^{1}H$ NMR spectra of organocobaloximes are generally very simple provided both the axial ligands are achiral, the four methyl groups on equatorial glyoximato ligand appear as a sharp 12 H singlet around 2.00-2.40δ. This, therefore, has been extensively used in monitoring the reactions of cobaloximes. Besides, $^{1}H$ NMR has also been used in mechanistic details and structural elucidation in solution phase.[98,124]

### 1.4.4 Electrochemistry

There are two important reasons why organocobalt complexes have been adopted by nature -

a) variability of coordination number, and

b) variability of oxidation state.

In vitamin $B_{12}$ and related ($Co^{III}$) complexes generally, (i) ($Co^{III}$) is ligated by two axial ligands (R, B); (ii) ($Co^{II}$) by one (B); and (iii) ($Co^{I}$) by one or none.[125,126] This

trend of decreasing coordination number has been qualitatively described by R-Co-B three centred, 4 - 5 - 6 electron, bonding metal orbital having substantial $d_z2$ character.[127,128]

1.4.4.A Electrochemical Reduction

The electrochemical reduction of cobaloximes has received little attention compared to Schiff's base $B_{12}$ models and data available for organocobaloximes are somewhat contradictory. Costa et al. have demonstrated with non-organocobaloximes that i) axial ligand has a marked effect on the $Co^{3+/2+}$ reduction potential, and ii) the nature of the equatorial ligand governs $Co^{2+/1+}$ reduction.[129-131]

Finke, Elliot and coworkers have observed that for alkyl and non-alkylcobaloximes, reduction is irreversible under all conditions of added ligand, solvent, temperature, etc., whereas vitamin $B_{12}$ derivatives undergo reversible electrochemical reduction.[132,133] However, LeHoang et al. found the electrochemical reduction of organocobaloxime to be reversible for most cases in DMSO.[134] Crumbliss and Morgan have obtained a set of data, which show that as the basicity of axial base ligand increases it becomes more difficult to reduce the cobaloximes, either electrochemically or chemically.[101]

### 1.4.4.B Electrochemical Oxidations

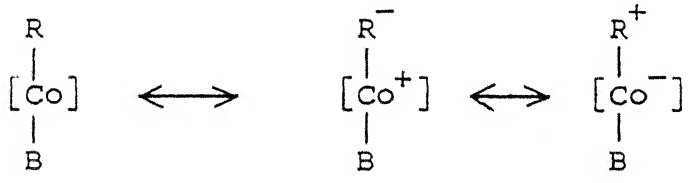
Organocobaloximes can be oxidised both electrochemically[135-142] and chemically.[135,143,144] EPR data suggests that the oxidised species contains ($Co^{IV}$).[135,145,146] Halpern et al. have estimated that the unpaired electron resides in a hybrid molecular orbital consisting primarily of 3d character with about 30% contribution from 4p orbital.[145] The oxidised complexes are unstable at room temperature and under solvent-assisted dissociation at low scan rates.[139] In the presence of a nucleophile, the decomposition of $R(Co^{IV})$ occurs via nucleophilic attack at the ligating carbon, yielding ($Co^{II}$) and R-nucleophile, with inversion of configuration.[142] One electron electrochemical oxidation of $RCo^{III}(dmgH)_2.H_2O$ with a variety of R group are found to correlate well with the Taft $\sigma^*$ parameter for R and with the $pK_a$ of RH. Recently, kinetic and thermodynamic data obtained as a function of R for reversible one electron oxidation of $RCo^{III}(dmgH)_2.H_2O$ in $CH_3CN$, reflect the importance of steric interaction of oxidation potentials.[140]

### 1.4.5 Stability of Cobalt-Carbon Bond

The nature of the carbon-cobalt bond has been of interest since the discovery of the structure of the vitamin $B_{12}$ coenzyme. The factors which control this stability of the cobalt-carbon bond have been discussed extensively. The essential structural

chemical and electrochemical parameters that govern the stability of Co–C bond in organocobalt complexes in general and cobaloximes in particular, are highlighted below.

Alkyl cobaloximes and alkylcobalamins have been found to be thermally stable organocobalt complexes. Alkylcobaloximes, for example, decomposes only at 200°C, pointing towards a stable Co–C bond. One possible way of expressing this axial Co–C bond stability may be through the resonating structure as follows:[33,34]



A knowledge of Co–C bond character has been derived from the changes in the orbital energies on the formation of the bond between a $d^7$ ($Co^{II}$) species and the organic radical. The d-orbital arrangement of the $d^7$ Co system has been considered to be intermediate between that for the $d^8$ system, in which the $d_{xy}$ orbital is belived to be appreciably higher in energy than the $d_z2$, and the $d^6$ system in which the $d_z2$ orbitals is of higher energy than the $d_{xy}$ orbital. As the bond formation involves the pairing of the $d_z2$ orbital with the carbon $sp^3$ orbital, the stability of the bond will depend upon the relative energies of these two orbitals and upon the relative energies of the $d_{xy}$

and $d_z2$ orbitals.[101] LCAO-MO calculations further indicate that interaction of $3d_z2$, $4p_z$ and 4s orbital of cobalt with carbon $sp^3$ orbital is mainly responsible for Co-C bond stabilization.[103] If the organic residue (R) is an $sp^2$ or sp hybridized carbon, then, additional interactions of the π-carbon orbital with $3d_{xz}$ and $3d_{yz}$ orbitals of cobalt lead to further stabilization of the axial bond.[101] Besides, any changes in the second axial ligand (B = usually base ligand) profoundly affects the stability of the Co-C bond trans to it (trans influence). Thus, more basic ligands have been shown to stabilize the organo-cobalt(III) complexes further. Like the axial ligand, the equatorial ligand also affects (cis-influence) the Co-C bond stability. This cis-influence, however, is much less pronounced than the trans-influence. Besides the electronic effects, the steric factors also play a marked role in the Co-C bond stability which has been established by X-ray crystallographic analysis.[101] An interesting linear relationship between the Co-C bond length and the number of substituents on the α-carbon to the metal has been observed.

The cobalt-carbon bond dissociation energy[110,141] of a number of organocobalt complexes and coenzyme $B_{12}$ (adenosyl cobalamin) has recently been estimated independently by Halpern et al.[141] and Finke et al.[110,147] The latter in a more exhaustive study, reported the reaction product, kinetic $\Delta H^{\neq}$, $\Delta S^{\neq}$ and

Co-C bond dissociation energy (BDE) for anaerobic and thermal decomposition of adenosyl cobalamin (Ado $B_{12}$) in aqueous solution. These studies reveal that the reaction proceeds via two competing pathways a) heterolytic Co-C cleavage to yield aquocobalamin, adenine and a sugar residue and b) competing Co-C homolysis to give Cob(II) alamin and 8,5'-anhydroadenosine. At pH 4 heterolysis dominates (88%) whereas at pH 7, homolysis dominates (~90%). Halpern's group on the other hand shows the cleavage mode to be homolytic only. Combining the above results and views with other data, Co-C BDE of base on form of Ado $B_{12}$ in water is estimated to be 30 $\pm$ 2 kcal/mole[110] and 26 kcal/mole.[141] Whereas it ranges from 17-25 kcal/mole for cobaloximes.

## 1.5 Reactions of Organocobalt Compounds

Organocobaloximes and related organocobalt complexes undergo four basic types of reaction:[33,36,40,61,148-152]

A. Cobalt-carbon bond cleavage

B. Insertion reactions

C. Reaction of a coordinated ligand

D. Ligand replacement reaction.

### 1.5.A Cleavage of the Cobalt-Carbon Bond

Co-C bond cleavage of organocobaloximes may be induced by,

i) reduction or oxidation of organocobaloximes,

ii) electrophilic, nucleophilic or radical attack at the group R,

iii) modification within the group R,

iv) charge transfer interaction of the macrocycle with additional reagents,

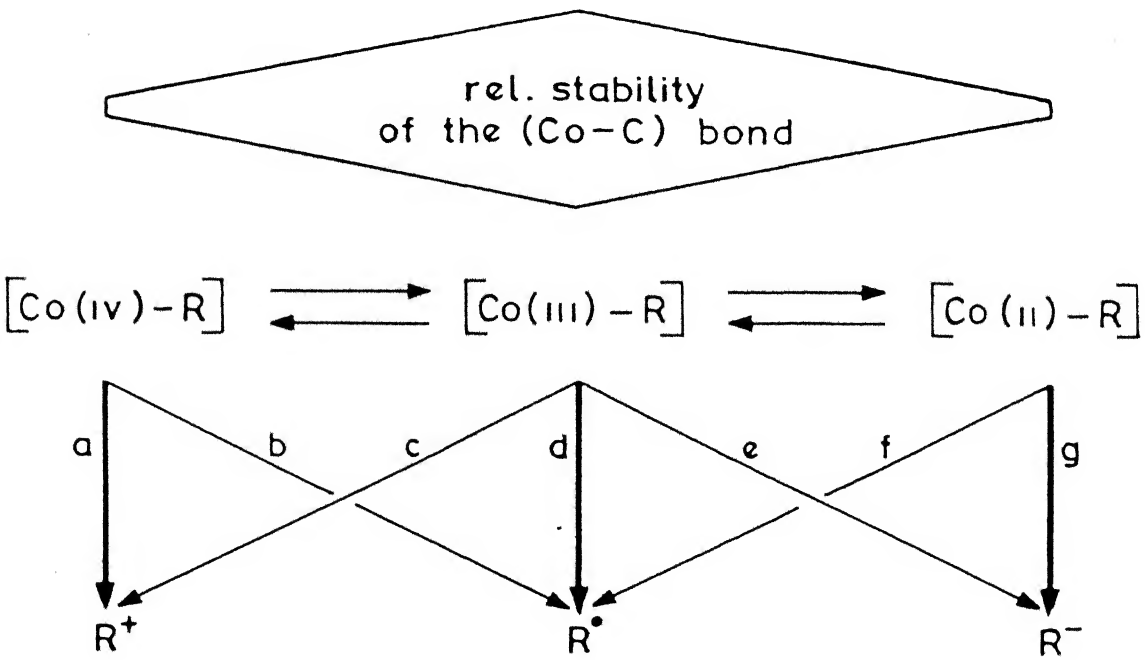
v) axial ligand exchange,

vi) light or heat, and

vii) steric interaction between macrocycle and alkyl group.

An actual cleavage is often caused by combined parameters. Scheme 1.3 depicts the formal routes of Co–C bond cleavage in different oxidation state:[128]

Scheme 1.3



The R group may react as an electrophile in $[R\text{-}Co^{IV}]$ (path a), as radical in $[R\text{-}Co^{III}]$ (path d), or as nucleophile in $[R\text{-}Co^{II}]$ (path g). However, reduction or oxidation of [R-Co] may allow decay routes b, c, e and f.

Owing to the instability of organocobalt complexes in the oxidation state ($Co^{II}$) or ($Co^{IV}$), the first order decay followed by trapping of free organic species by the reagent is favoured.

Compared to ($R\text{-}Co^{III}$) compounds, the ($R\text{-}Co^{II}$) compounds are less stable and the stability depend very much on the nature of the macrocycle,[153] the alkyl moiety and the axial base. The nature of the reduction products[154,155] points to the radical and anionic mechanism (path f or g). It is very difficult to distinguish between path f and g, because the free radicals so formed on reduction may further be reduced to anion.

The one electron oxidised complexes ($R\text{-}Co^{IV}$) have a short lifetime and can be cleaved by two pathways:

Path a: Nucleophilic attack on ($R\text{-}Co^{IV}$). This occurs with inversion of configuration at the cobalt bound carbon (2nd order rate constants). Intramolecular nucleophilic displacement involving the macrocycle has also been observed on the basis of kinetic results.[138,156]

Path b: Direct homolytic displacement of ($Co^{III}$) in ($R\text{-}Co^{IV}$).[157]

Organocobalt(III) complexes are usually stable enough to be isolated. The cleavage of Co-C bond in organocobalt(III) complexes is a consequence of an attack by a reagent in a bimolecular reaction. Redox reactions between oxidizing or reducing reagents and $[R\text{-}Co^{III}]$ may compete with bimolecular substitution reaction. In general, the cleavage can be either heterolytic or homolytic and is broadly encompassed into the following three categories:

<u>Path c</u>: i) $R\text{-}Co^{III} + X^- \longrightarrow RX + (Co^I)^-$

ii) $(^*Co^I) + R\text{-}Co^{III} \longrightarrow {}^*Co^{III}\text{-}R + (Co^I)^-$

<u>Path d</u>: i) $R\text{-}C^{III} + X^\bullet \longrightarrow RX + (Co^{II})$

ii) $R\text{-}Co^{III} + (^*Co^{II}) \longrightarrow {}^*Co^{III}\text{-}R + (Co^{II})$

<u>Path e</u>: i) $R\text{-}Co^{III} + X^+ \longrightarrow RX + (Co^{III})^+$

ii) $R\text{-}Co^{III} + (\ Co^{III}) \longrightarrow Co^{III}\text{-}R + (Co^{III})^+$

<u>Path c</u>: Cleavage by nucleophiles

A few nucleophilic displacement reactions at cobalt have been studied. Representative examples are shown in Scheme 1.4.

In principle, for such reactions the nucleophile $X^-$ must have a strong affinity towards the α-carbon bound to cobalt. The possible reversibility depends upon the ability of $(Co^I)$

species as a leaving group, the incoming nucleophile as

Scheme 1.4

Nucleophilic Displacement at Cobalt-Carbon Bond

$$CH_3(Co^{III}) + X^- \longrightarrow CH_3X + (Co^I)^-$$

($X^-$ = $Cl^-$, $Br^-$, $I^-$, $CN^-$, $RS^-$, $NRPh^-$ etc.)

$$H_2C{=}C{=}CH(Co^{III}) + BH_4^- \longrightarrow H_2C{=}C{=}CH_2 + (Co^I)^-$$

$$OH(Me)CHCH_2(Co^{III}) + OH^- \longrightarrow Me_2CO + (Co^I)^- + H_2O$$

$$H_3C{-}C(=O)(Co^{III}) + NH_2OH \longrightarrow CH_3CONHOH + (Co^I)$$

$$H_3C{-}C(=O)(Co^{III}) + NH_2OH \longrightarrow CH_3CONHOH + (Co^I)$$

$$CH_3(Co^{III}) + (Co^I(chgH)_2Py)^- \rightleftharpoons CH_3Co^{III}(chgH)_2Py + (Co^I)^-$$

[Co = $Co(dmgH)_2Py$; chgH = cyclohexylglyoxime monoanion]

well as their carbon basicities. When the reactions are carried out under aerobic conditions, oxygen removes ($Co^I$) from solution and reaction becomes faster. In contrast, no reaction should occur in the absence of oxygen. Since reactions in both aerobic and anaerobic conditions are reported, ambiguity, therefore, prevails about this class of reactions. Though all the examples given in scheme 1.4 are categorized under the broad heading of 'Nucleophilic displacement at Co-C bond', there is little evidence available, except for when X = $RS^-$, for such displacement reactions. This is expected since $(Co^I)^-$ must surely be a very poor

leaving group, for example number 3 reaction in scheme 1.4 is very unlikely to be a nucleophilic displacement of ($Co^{I}$) by $H^{-}$:. Similarly, number 4 reaction must be an example of a base catalysed decomposition i.e. $OH^{-}$ is a base in this reaction and not a nucleophile. Nucleophilic metal to metal exchange reactions (reaction 6) however, have been conclusively proved to be of $S_N2$ type with inversion taking place at the cobalt bound to α carbon of the substrate complex.[158] The base catalyzed decompositions of methyl,ethyl and 2-alkoxyethylcobaloximes have been studied by Brown et al.[55,159-163] and different mechanisms have been proposed for different cobaloximes. Schrauzer's group has reported the cleavage of 2-hydroxyethylcobalt chelates by alkali to $Co^{I}$ chelates and acetaldehyde and dealkylation of alkylcobalt(III) by mercaptide ions to form dialkylsulphides.[60,164,165] The dealkylation of alkylcobalt(III) complexes is readily accomplished with Co(I) or Rh(I) supernucleophile in what amounts to alkyl exchange between reduced metal species. From kinetic study an $S_N2$ reaction has been proposed.[158,167]

Path d: Homolytic cleavage of Co-C bond

Homolysis of the Co-C bond in coenzyme $B_{12}$ is widely accepted to be a primary key step in its mechanism of action. Much research efforts have been devoted to the study of homolytic cleavage of Co-C bond.

The homolysis of organocobalt(III) complexes, $R(Co^{III})$, results in the cleavage of Co–C bond giving rise to a caged radical pair $R^{\bullet}(Co^{II})$, which then further leads to the formation of alkanes and/or alkenes.[166] Since the organic and inorganic radicals are easily generated this way, it has led to the thought that how can these radical fragments react directly or indirectly with the organometallic substrates. Since the homolytic displacement reactions at carbon centre are rarely[150,168,169] observed, it has generated lot of interest among scientists to study these reactions in organocobaliximes. Recently a number of such studies between σ-bonded organometallic complexes with organic or organometallic free radical precursors have been reported[150] as illustrated below:

$$XY + RMLn \longrightarrow RY + XMLn$$

MLn = $Ir(Co)P_2X_2$, $Rh(Co)P_2X_2$, $Co(dmgH)_2B$

X = Br, Cl

P = $PPh_3$, $PMe_2Ph$

B = Pyridine, imidazole

R = Alkyl, allyl, allenyl, etc.

Y = $CCl_3$, $CCl_2CN$, $CCl_2CHO$, $CCl_2Co_2R$, $ArSO_2$, $ArSO_2NMe$, PhS, PhSe.

The key step in the above reactions involves the homolytic displacement of a lowvalent metal complex by attack of a C, N or S centred radical at unsaturated or saturated carbon of the organic ligand of the organometallic complex.[150,170-173] The overall reaction sequence is outlined below:

$$\text{Initiation} - \quad RMLn \rightleftharpoons R^{\bullet} + M^{\bullet}Ln$$

$$\text{Propagation} - \quad M^{\bullet}Ln + XY \longrightarrow XMLn + \dot{Y}$$

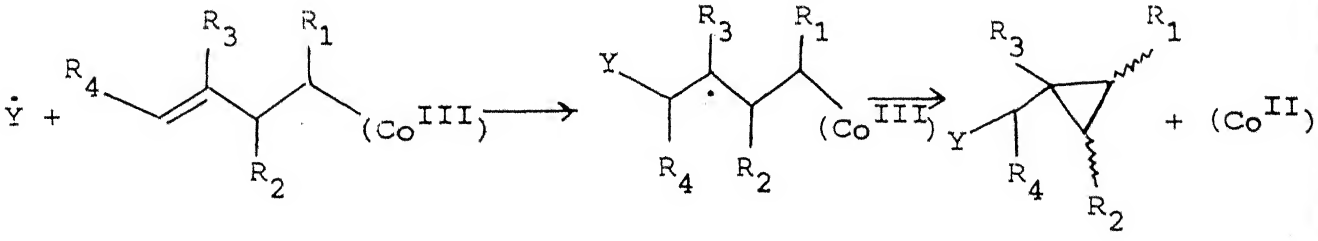
$$\dot{Y} + RMLn \longrightarrow RY + M^{\bullet}Ln$$

$$\text{Termination} - \quad \dot{Y} + \dot{M}Ln \longrightarrow YMLn$$

$$\dot{Y} + \dot{Y} \longrightarrow Y_2$$

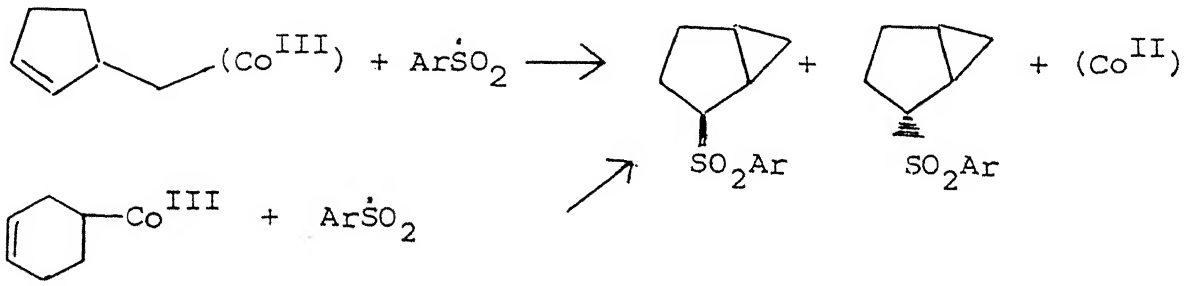
In general, the attack of $\dot{Y}$ takes place at the terminal carbon of the unsaturated organic group like allyl, allenyl, hexenyl etc. However, exception to this is also reported.[150]

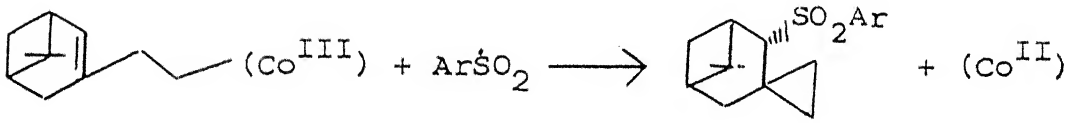
A number of reactions have been described[170-172] in which the attack of the free radical at the unsaturated carbon centre is followed by the intramolecular homolytic displacement at the saturated α-carbon atom.



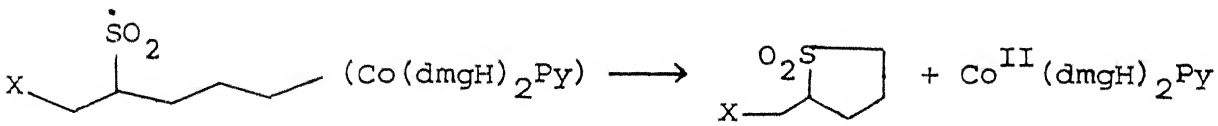

($\dot{Y}$ = $CCl_3$, $ArSO_2$, CNCHBr etc.)

Spiro and fused cyclopropane systems have been synthesized[150] by the reaction of appropriate cycloalkenyl cobaloximes with free radical precursors by similar $S_H2$ reactions:




The formation of sulpholanes by the intramolecular attack of remote sulphonyl radical on the α carbon of the substituted alkyl cobaloximes ($S_Hi$) has been described.[174]




Free radicals, generated by Co–C bond homolysis (by photochemical methods) have recently been trapped with many useful functional groups.[175] Scattered examples of the study by captodative

radicals with organocobaloximes are also noted in literature.[176]

Many aspects of the homolytic studies in organocobaloximes are similar to that of the organocobalamins and these will be discussed in detail under Section 1.7.

Path e: Cleavage by electrophiles

Among several types of σ-bonded organotransition complexes, the reactions of organocobalt(III) and organoiron(II) complexes with electrophiles are less understood and no unified mechanism has emerged so far. This is because of the seemingly endless variety of reactions they undergo, and in case of organocobalt complexes, their importance in relation to the chemistry of coenzyme $B_{12}$.[34]

The reaction possibilities are: synchronous attack of the electrophile with cleavage of carbon-metal bond, reactions in which the carbon-metal bond is modified, reactions in which there is little influence of or on the carbon-metal bond.

Thus a variety of electrophilic reagents viz., protonic acids, metal ions, halogen molecules etc. induce Co-C bond cleavage as illustrated in scheme 1.5.

The mechanism of the acid catalysed decomposition of β-hydroxyalkylcobalt(III) complexes has been studied in detail.[54,177-179a] Thus formation of ethylene from $HOCH_2CH_2Co^{III}$

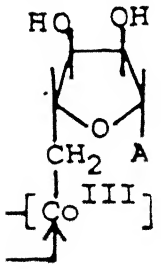
## Scheme 1.5

Cleavage of Co-C bond by electrophiles

### Acid catalysed cleavage

$$ROCH_2CH_2(Co^{III}) \xrightarrow{H^+} H_2C{=}CH_2 + ROH + (Co^{III})^+$$

(R = H, Me, Et, etc.)

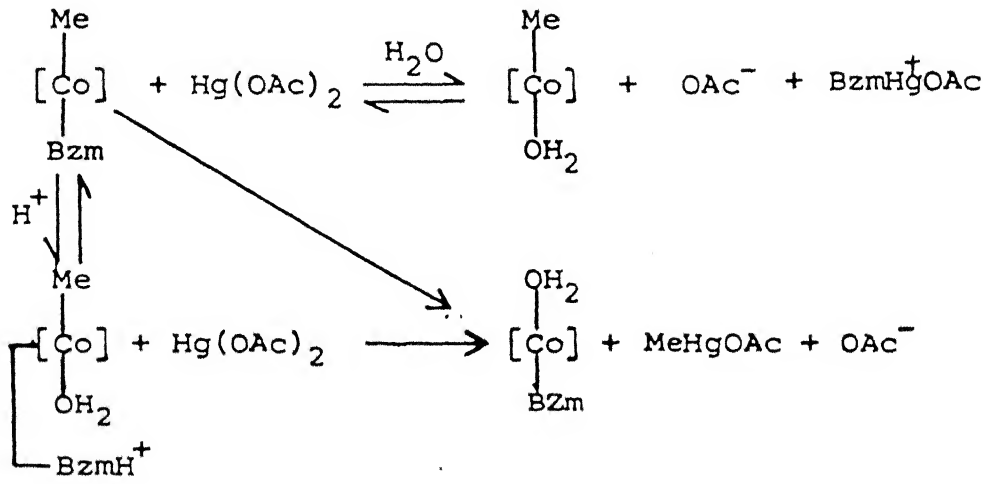


$$\xrightarrow{H^+} B_{12s} + H_2C{=}CHCH(OH)CH(OH)CHO + A$$

(A = adenine)

### Cleavage by metal electrophiles

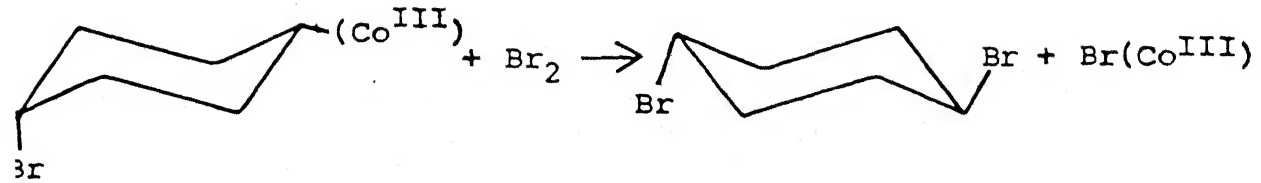
$$cis\text{-}PhCH{=}CH(Co^{III}) + Hg(OAc)_2 \longrightarrow cis\text{-}PhCH{=}CH(HgOAc) + AcO(Co^{III})$$



### Halogenation

$$(S)\text{-}(+)C_6H_{13}CHMe(Co^{III}) + Br_2 \longrightarrow (R)\text{-}(-)C_6H_{13}CHMeBr + Br(Co^{III})$$

$$+ C_6H_{13}CHBrCH_2Br + C_5H_{11}CHBr\ CHMeBr$$



is beleived to proceed via an intermediate $\pi$-complex between cobalt and ethylene. On the other hand, $OHCH_2(CH_3)CHCo^{III}$ undergoes reversible isomerisation to $CH_3CH(OH)CH_2(Co^{III})$ prior to alken release.

The mechanism of Co-C bond cleavage by metal ions has been of interest in view of the methylcobalamin dependent toxic methyl mercury formation.[179b]

Halogenation study of organocobaloximes, in particular, has been confined mainly to alkylcabaloximes and their reaction with ICl and $I_2$[33,149,151,180,181] and their mechanistic elucidations are attempted from kinetic considerations only.[182d]

Several mechanisms for Co-C bond cleavage are reported,

(i) direct electrophilic substitution on the α carbon,

(ii) direct radical attack on α carbon,

(iii) oxidative dealkylation process,

(iv) single electron transfer mechanism.

Compared to alkylcobaloximes, the halogenation of benzylcobaloxime appears to be more complicated. Apart from the above four types of mechanism an additional feature of benzyl cobaloxime is that the benzene ring is also susceptible to electrophilic substitution. Each one of these mechanisms finds support from the literature. However no clearcut one mechanism has emerged so far. Recently in our laboratory a detailed study of

halogenation on a carefully designed set of substituted benzyl-cobaloximes have been done.[183,203] A brief account of the highlights of this study is given below:

(1) A clear variation of mechanism with change in R group in $4\text{-}RC_6H_4CH_2Co^{III}(dmgH)_2Py$ has been established, i.e. from direct electrophilic to oxidative dealkylation to electrophilic.

(2) Chlorination and bromination have a different mechanism from that of iodination.

(3) In some newly synthesized heteroaromatic methyl cobaloximes, it has been found that the aromatic ring is activated enough to undergo a preferential ring substitution by halogen as compared to Co-C bond cleavage. The substituent effect of $-CH_2Co^{III}(dmgH)_2Py$ group is found to be more than the methoxy group.

(4) The formation of benzyl ethers of dimethylglyoxime, a characteristic decomposition product of RCo(IV) points to the intermediate formation of cobalt(IV) species in solution.

(5) Meta-substitution (Me, OMe) is much more effective in causing ring substitution as compared to the para-substitution.

(6) A slight change in the electron density at cobalt changes the course of reaction further.

Cleavage of a number of β styryl cobaloximes by halogens has been extensively studied.[52] The method finds an excellent use for the synthesis of β styryl halides of high isomeric purity. Many other electrophiles like, 2,4 dinitro benzene sulphenyl chloride,[182a], 1,3 benzodithiolylium tetrafluoroborate[182b] tetracyano ethylene,[92] nitrosyl chloride[182c] etc. have also been studied.

### 1.5.B Insertion Reactions

Studies on the photochemical and thermal insertion of molecular oxygen, sulphur dioxide and sulphur into Co-C bond in many alkyl, allyl, vinyl, allenyl, aryl and benzylcobaloximes have been carried out.[33,35,36] The reaction conditions vary from irradiation of a solution of organocobaloxime at low temperature (ca. -40°C) to heating at 40-60°C. Sulphur dioxide insertions with liquid $SO_2$ in sealed tube under irradiation have also been carried out. The yield of the product is nearly quantitative in most of the cases.

In view of kinetic,[184,185] ESR[186,187] and stereochemical studies[188,189] the participation of free radicals has been confirmed in such reactions and the following two alternative mechanisms have been proposed:

Mechanism 1:

$$R(Co^{III}) \underset{}{\overset{h\nu/\Delta}{\rightleftharpoons}} (Co^{II}) + \dot{R} \xrightarrow{X} (Co^{II}) + R\dot{X} \longrightarrow RX(Co^{III})$$

Mechanism 2:

$$R(Co^{III}) \rightleftharpoons R^{\bullet} + (Co^{II})$$

$$(Co^{II}) + X \longrightarrow X(Co^{II})$$

$$X(Co^{II}) + R(Co^{III}) \longrightarrow RX(Co^{III}) + (Co^{II})$$

$$(Co^{II}) + X(Co^{II}) \longrightarrow (Co^{III})X(Co^{III})$$

($X = O_2$, $SO_2$)

However, in few cases the insertion reaction has led to the formation of organic or inorganic byproducts along with the expected compound.[173a,190]

$$PhCH(Me)(Co^{III}) \xrightarrow[O_2,\ 30^{\circ}C]{CH_2Cl_2} Ph(Me)CHOO(Co^{III}) + Cl_2CH(Co^{III}) + ClCH_2(Co^{III}) + Cl(Co^{III})$$

$$Me_2C{=}CHCH_2(Co^{III}) \xrightarrow{SO_2} CH_2{=}CHC(Me)_2SO_2(Co^{III}) + Me_2C{=}CHCH_2SO_2C(Me)_2CH{=}CH_2$$

Decomposition studies of the inserted cobaloximes under various conditions have been carried out, which give organic

products from an initial cleavage of the cobalt-axial ligand bond[191-193] and are of interest as a synthetic route e.g. synthesis of alkyl hydroperoxides.[194]

$$RR'CHCOO(Co^{III}) \xrightarrow[\text{Methanol}]{NaBH_4} RCHOHR' + OH(Co^{III})$$

$$PhCH{=}CHCH_2SO_2(Co^{III}) \xrightarrow[H_2O]{SO_2} PhCH{=}CHCH_3 + O_3S(Co^{III})$$

$$RS_4(Co^{III}) \xrightarrow{h\nu/\Delta} RS_4R + (Co^{III})S_4(Co^{III})$$

Although oxygen and sulphur dioxide insertion reactions have been pursued in great detail, a few other insertion reactions have also been attempted:[35]

$$R(Co^{III}) \xrightarrow[h\nu]{R'OH,\ CO} R{-}O{-}\overset{\overset{O}{\|}}{C}{-}(Co^{III})$$

$[(Co^{III}) = Co(salen)H_2O,\ Co(acacen)H_2O]$

A case of photochemical substitution reaction of alkylcobaloximes by hydroperoxides leading to dioxy products has been reported.[195]

$$R(Co^{III}) + 2\ R'{-}OOH \xrightarrow[C_6H_6/N_2]{h\nu} R'OO(Co^{III}) + ROOR'$$

However, a reinvestigation of the above work with $(Co^{II})$ and

tert-butyl hydroperoxide suggests the participation of $Me_3COO^{\bullet}$ and $Me_3CO^{\bullet}$ radicals in a chain sequence:[196]

$$2\ Me_3COOH + 2(Co^{II}) \longrightarrow HO(Co^{III}) + Me_3COO\text{-}(Co^{III}) + Me_3COH$$

1.5.C Reaction of the Coordinated Ligands

In organocobaloximes, both axial and equatorial ligands undergo very interesting reactions. These reactions can be broadly classified into three categories.

i) protonation, deprotonation at axial or equatorial ligand sites:

Cobaloximes having acidic sites in its axial and equatorial organic ligands get converted to corresponding conjugate bases in alkaline medium.[36,88]

$$HOOCCH_2(Co^{III})H_2O \rightleftharpoons [OOCCH_2(Co^{III})H_2O]^- + H^+$$

$$R(Co^{III})(OH_2) + {}^-OH \rightleftharpoons [R(Co^{III})(OH)]^- + H_2O$$

$$PhCH{=}CH(Co^{III}) + CH_3Li \longrightarrow Li^+[PhCH{=}CHCo(dmgH)(dmg)Py]^- + CH_4$$

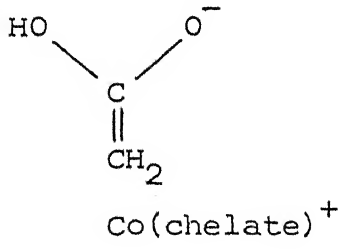
For carboxylproton dissociation from (carboxyethyl) (ligand) cobaloximes with 15 different axial ligands, it has been found that the $\sigma$ values (inductive substituent parameter) are directly proportional to the measured proton basicity of the trans axial ligands.[197]

On the other hand the protonation of the equatorial dimethylglyoximate ligand has also been reported[198]:

$$R(Co^{III})(OH_2) + \text{aq. HCl} \rightleftharpoons [RCo(dmgH)(dmgH_2)Cl] + H_3O^+$$

Recently it has been found that the first equatorial oxime protonation increases the rate of dissociation of pyridine by 3 orders of magnitude while the second equatorial oxime protonation increases the rate by 10 fold. It is postulated that the transition states for ligand dissociation from the cationic complexes are substantially stabilized by intramolecular proton transfer from the protonated equatorial oxime functionalities to the departing axial ligand.[199]

The acidities of cobaloximes largely depend upon the inductive and hyperconjugative effect of $[-CH_2(Co^{III})B]$ moiety and also upon the extent of $\sigma-\pi$ conjugation as follows:




The electron donating inductive effect of cobaloxime moiety is usually very high. Furthermore, the hyperconjugative effect of the cobaloxime substituent $[-CH_2(Co^{III})X]$ in benzyl

cobaloximes decreases in the order[200]; ($X = CN^- > NO_2^- > N_3^- \gg Cl^- \gg Br^- > SCN^- > I^-$)

ii) reactions involving β-carbon of the axial ligand:

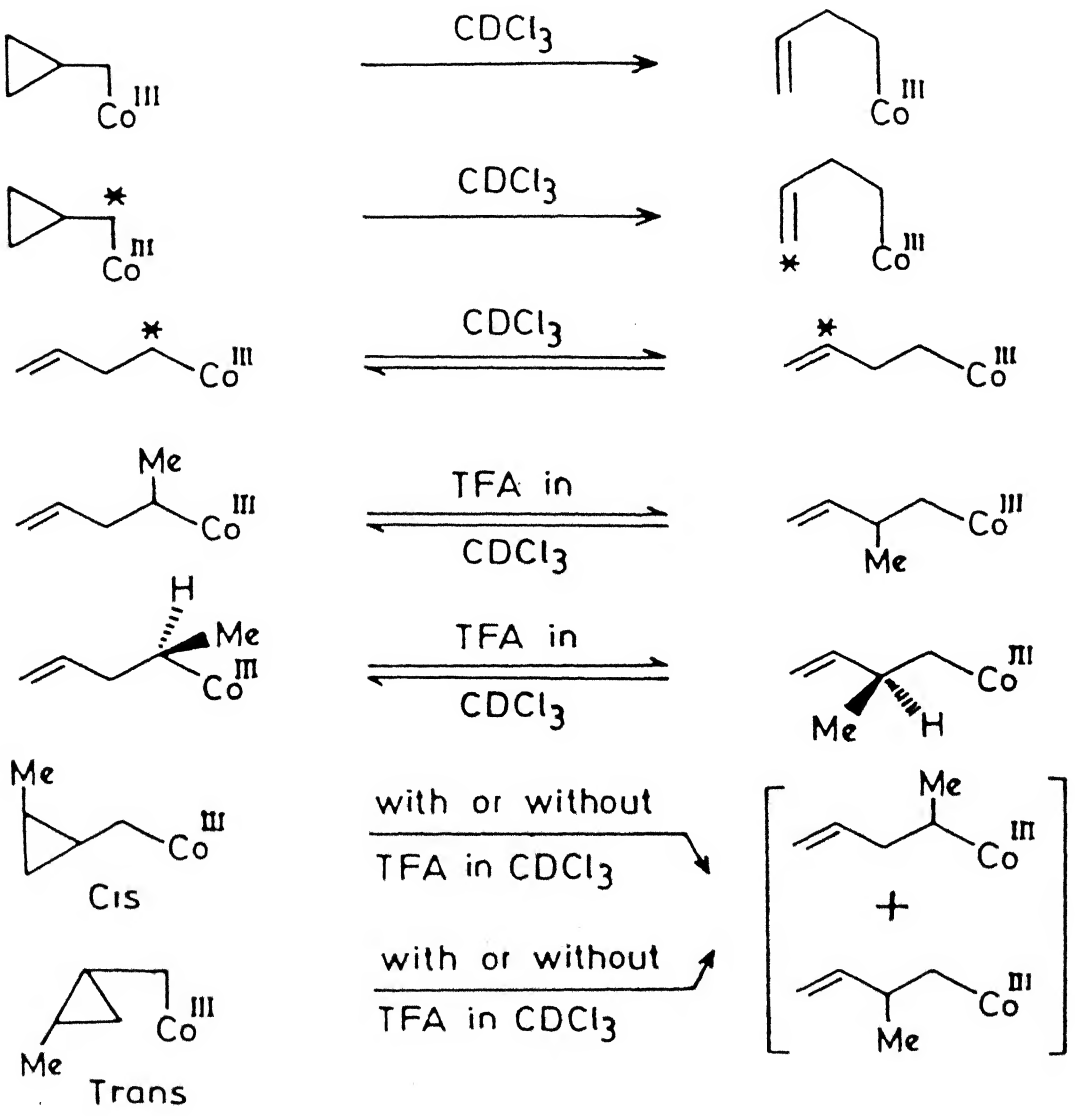
The β carbon atom in complexes of the type $ACOCHRCH_2(Co^{III})$ is very reactive and readily affords the solvolysis product, $OHCHRCH_2(Co^{III})$ or $R'ORCHCH_2(Co^{III})$ in water or alcohol.[89] Many reactions of this type are discussed in Sec. 1.3.1.D.

Besides, kinetic studies have been done on (β hydroxy-alkyl) cobaloximes in acid solution. β Hydroxy ethyl derivative evolves ethylene, whereas corresponding n propyl and isopropyl derivatives undergo reversible isomerization prior to olefin release.[178]

iii) A number of reactions have been reported by Johnson[201] and Golding,[202] in which the axial organic ligands in cobaloximes undergo σ-π migration to give new cobaloximes as illustrated in scheme 1.6. These reactions are of considerable synthetic interest and have played a convincing role in the model studies of $B_{12}$-dependent diol dehydrase and α-methylglutarate mutase reactions as described in Sec. 1.3.1.D.

# Scheme 1.6

## σ - π Migration



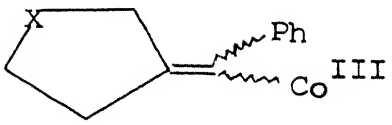

$Co^{III}$ = $Co(dmgH)_2$ Py

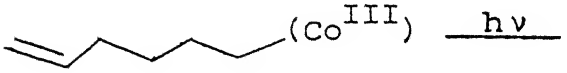
TFA = $CF_3COOH$

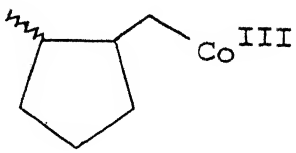
Very recently, Johnson has reported a number of reactions in which substituted alkyl cobaloximes, on photolysis, undergo rearrangement to more stable substituted alkyl- or alkenyl-cobaloximes.[204] The rearrangements have been rationalised in terms of a reversible homolysis of the cobalt-carbon bond, rearrangement of the organic radical and recapture by the ($Co^{II}$) fragment to give new cobaloximes that are more stable to irradiation than their precursors:

$$PhC{\equiv}CCH_2X(CH_2)_n(Co^{III}) \xrightarrow[Py]{h\nu}$$

($X = CH_2$, $n = 1, 2, 3$; $X = O$, $n = 2, 3$)




## 1.5.D Ligand Substitution Reactions

The most important class of the ligand substitution reactions in cobaloximes involves direct displacement of an axial base ligand by another base ligand of a cobaloxime moiety as shown in the following examples:[33,204]

$$R(Co^{III})B + B' \longrightarrow R(Co^{III})B' + B$$

(B = $H_2O$; B' = Py, imidazole, $PPh_3$ etc.)

$$R(Co^{III})H_2O + CNX(Co^{III})B \longrightarrow R(Co^{III})CNX(Co^{III})B + H_2O$$

(X = S, Se; B = Py, piperidine etc.)

An axial base is often replaced by another ligand having stronger affinity for cobalt.[34] For bases having different donor atoms the affinity decreases in the order P > N > S > O while, for bases with same donor atom, such as pyridine and its derivatives, the affinity order follows that of the basicity of the ligands. It is noteworthy that the substitution of a base ligand is not only dependent upon the incoming ligand but also on the trans-influence of the axial organic ligand over the axial base ligand.[101] This effect tends to labilize the cobalt-base bond and may even result in the formation of a five coordinated species by the elimination of the base. The two effects as discussed above, have been very well demonstrated by kinetic studies. Thus, the first order rate of dissociation of trimethylphosphite from $[R(Co^{III})P(OMe)_3]$ decreases in the order: R = $Me_3SiCH_2$-> $-CH_2F$> $-CHF_2$> $-CH_2Cl$> $-CF_3$= $-CHCl_2$= $-CH_2Br$ > $-CHBr_2$.[205] On the other hand, the rate of axial base exchange in $[CH_3(Co^{III})B]$ decrease in the order of B = $CH_3CN$=$Ph_2SO$= $Me_2SO$> $Me_2S$> $Me_3N$> $Et_3N$> $Ph_3P$> $P(OMe)_3$.[206]

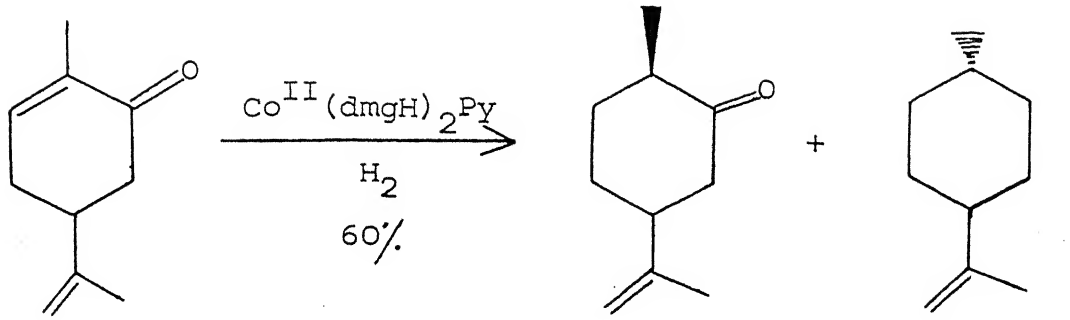
The substitution reactions by $CNX(Co^{III})B$ group have been studied in some detail.[207] The tendency in the formation of the pseudo halide bridged dimer $R(Co^{III})CNX\ (Co^{III})B$ decreases with CNX = NC > NCS > NCSe > SCN >> OCN. However, in the presence of trace amount of cobaloxime(II); oligomers of the type $R(Co^{III})\{CNX(Co^{III})\}_n[CNX(Co^{III})B]$ have been formed.

## 1.6 Organocobaloxime as a Potential Synthetic Precursor

Though organocobaloximes appear to be the best model for vitamin $B_{12}$ coenzyme studied so far, enormous useful and interesting physical and chemical studies reveal its chemistry as more of an independent area rather than as model for vitamin $B_{12}$ chemistry. Furthermore, with the recent observations that cobaloximes can be used as potential industrial catalysts and synthetic inorganic mediators in carrying out a number of interesting and useful chemical transformations, a new field of research is emerging. Few representative examples of this area are given below.[128,208]

### A) Hydrogenation of olefins

Cobaloximes offer selective, specific and mild conditions for hydrogenation of activated or conjugated olefins (Eqn. 1):[63]




.. (1)

Asymmetric induction during catalytic hydrogenation has been observed in the presence of cobaloxime(II) having optically active bases (Eq. 1, quinine), for example, α-phenylacrylophenone affords 1-methyl-2-oxo-stilbene in enantiomeric excess of 49%.[209c]

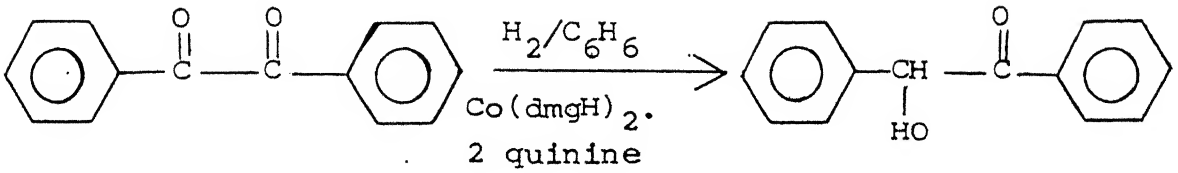
B) Reduction of functional groups

Reduction of several functional groups like C-halo, $NO_2$, NO, C=NOH, C=N-R, N≡N- by $[Co^{I}(dmgH)_2Py]^-$ generated in situ, has been reported.[209a,b]

$$p\text{-}NO_2C_6H_4CH{=}CH\ CO_2Me \xrightarrow[CH_3OH/\ Co(dmgH)_2.2H_2O]{H_2/1\ hr} p\text{-}NH_2C_6H_4CH_2\text{-}\underset{\displaystyle CO_2Me}{\underset{|}{CH_2}} \qquad \text{.. (2)}$$

$$PhHC{=}NSO_2Ar\text{-}CH_3\text{-}4 \xrightarrow[H_2]{Na[Co(dmgH)_2Py]} PhCHNHAr\text{-}CH_3\text{-}4 \qquad \text{.. (3)}$$

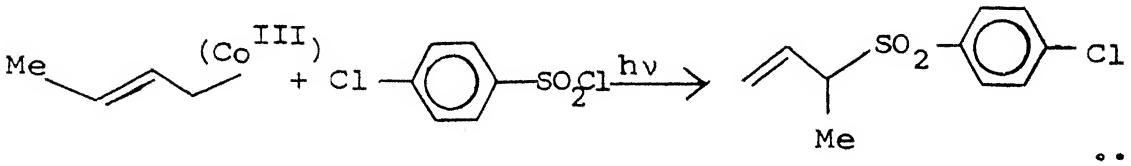
Asymmetric induction as in Eqn. (1) is also reported (Eqn. 4):




S(+)benzoin (98%) ..(4)

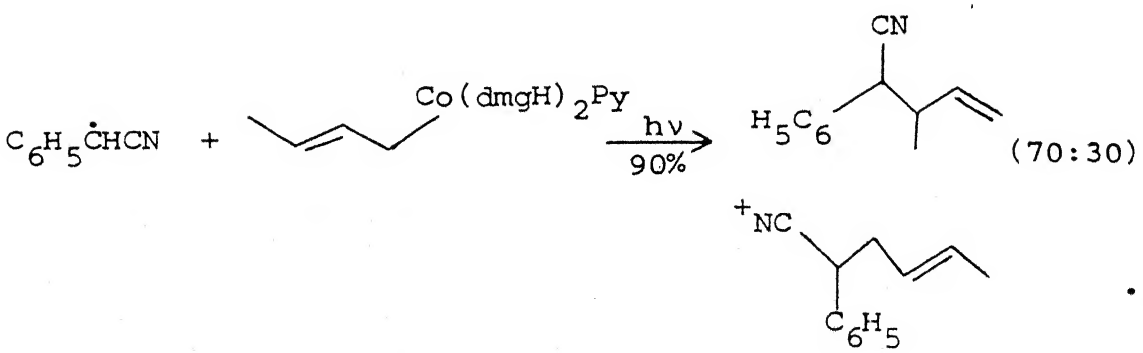
C) Intermolecular formation of aliphatic C-C bond

Cobaloximes can be employed as precursor for the synthesis of several organic compounds. Thus allyl, allenyl, butenyl etc. Cobaloximes when reacted with organic radicals (discussed in Sec. 1.5.A.d) give rise to organic products by $S_H2$ or $S_H2'$ reactions.[150,210,211]




.. (5)

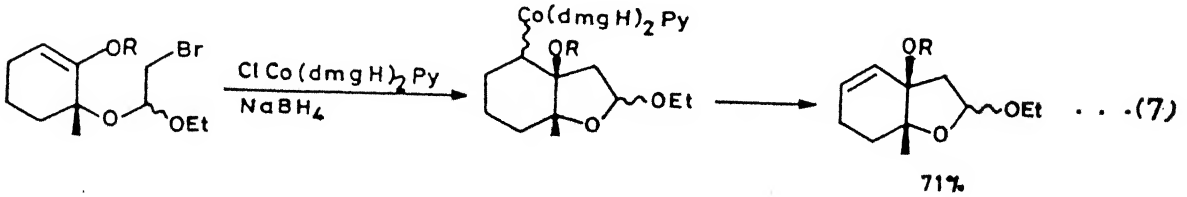
Allylation of nitriles has recently been reported by Gaudemer et al. (Eqn. 6):[176]

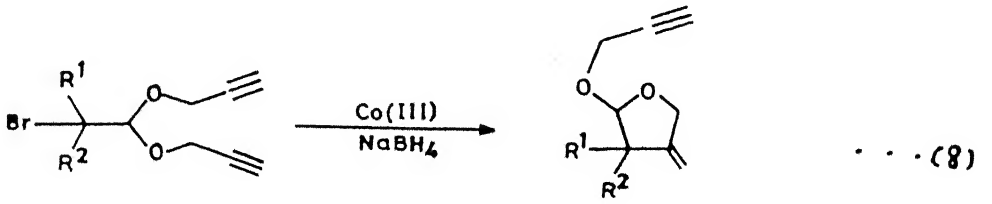


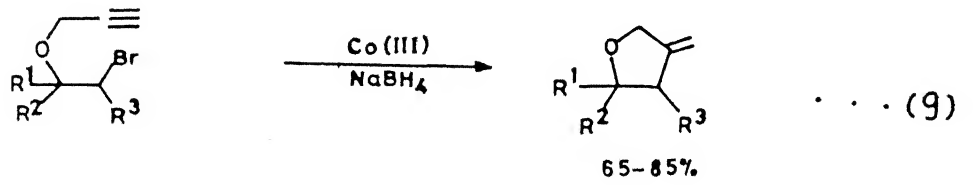

.. (6)

D) Intramolecular formation of aliphatic C-C bond

A number of reactions are recently reported in which an initial electron transfer from ($Co^{I}$) to an organic halide generates a free radical which rearranges to give cyclised product (Eqns. 7-9):[213-215]




## 1.7 Coenzyme $B_{12}$ Chemistry: Cobaloxime as Model

In 1964 Schrauzer et al.[29] reported that the reaction of the cobalt atom in vitamin $B_{12}$ can be simulated with much simpler organocobalt complexes. Since then, an enormous studies have been done on various organocobalt complexes and it has been

established that organocobaloximes in spite of their wide structural differences to coenzyme $B_{12}$ show many electronic, electrochemical and chemical similarities to the latter and its derivatives. Our understanding of the chemistry of vitamin $B_{12}$ coenzyme, as it stands today, is largely an outcome of the study of its model compounds. Some aspects of the relationship of $B_{12}$ model to $B_{12}$ biochemistry have recently been reviewed.[34,216] Prior to a consideration of the relevance of cobaloxime chemistry to $B_{12}$ biochemistry, it is worthwhile to highlight some aspects of the latter.

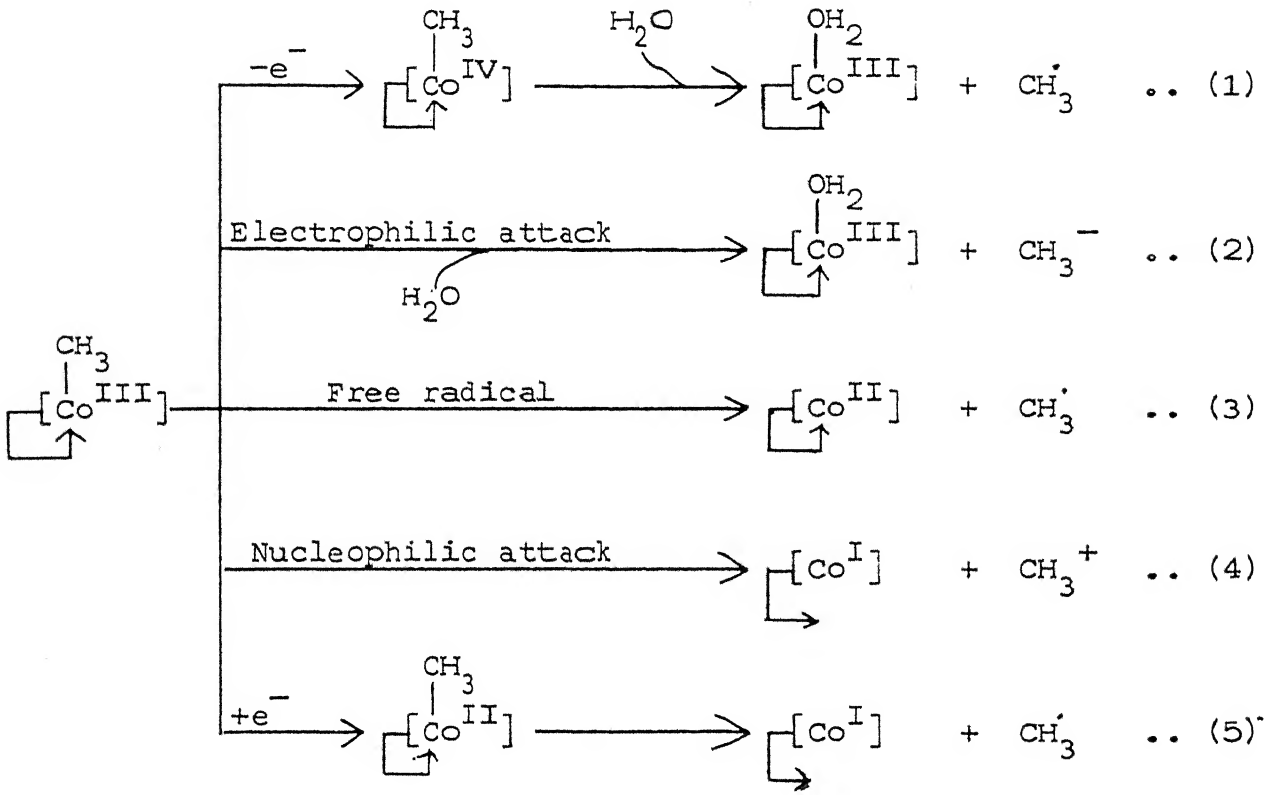
In vitamin $B_{12}$ mediated enzymatic reactions the correnoids act in association with a protein. Thus, correnoids are the co-factors or coenzymes for all these enzymatic processes which can be divided into two sub-groups,[148,217] those mediated by i) methylcobalamin ($CH_3Cbl^{III}$ or $CH_3-[Co^{III}]$ and ii) 5'-deoxyadenosylcobalamin ($AdCH_2Cbl^{III}$ or $AdCH_2-[Co^{III}]$, the so called $B_{12}$ coenzyme.

i) Methylcobalamin dependent processes:

Based on structural and kinetic studies, five alternative pathways have been suggested that lead to methyl transfer from methylcobalamin (Scheme 1.7).[218] The validity of the proposed mechanisms is still open to question unless rigorous proof is obtained from enzymatic studies.

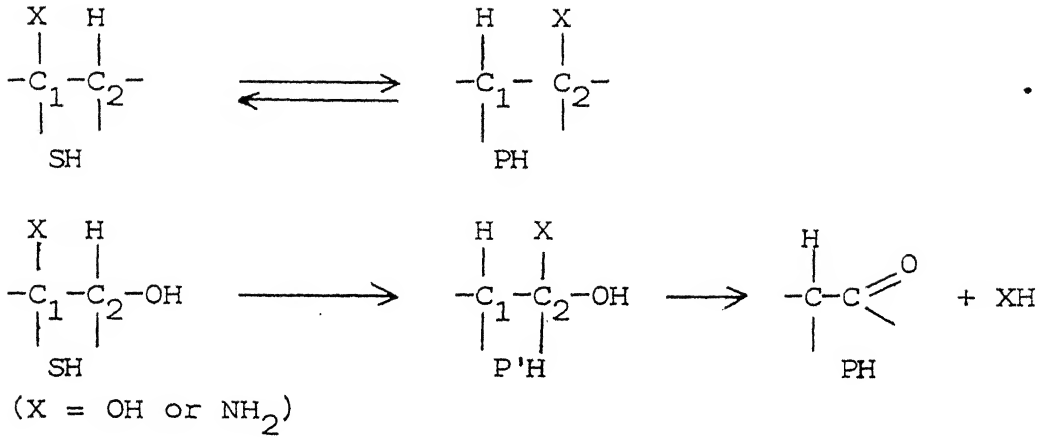
Scheme 1.7

(Methyl transfer from Methyl cobalamin)




ii) 5'-Deoxyadenosyl cobalamin dependent processes:

A common feature of these reactions, depicted by (eqn. 1), is the 1,2-interchange of hydrogen atom and another substituent [X = $NH_2$, $CH(NH_3^+)CO_2^-$, C(=O)SCoA, C = $(CH_2)COOH$ or $CH(NH_2)COOH$ ] on adjacent carbon atoms of the substrate.[212,219]

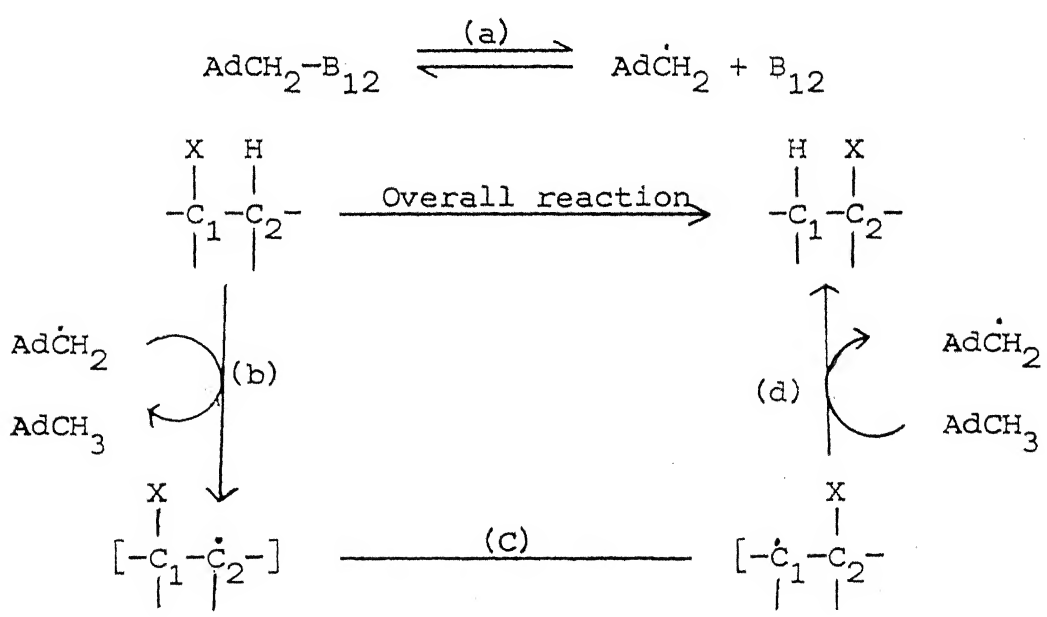


.. (1)

(X = OH or $NH_2$)

Although the essential features of the overall mechanism of such processes, Outlined in scheme 1.8,[34,99,220,244] have convincing evidences and has been accepted by many workers as a remarkable working hypothesis, nevertheless, a few other alternative proposals have also been worked out through model studies.[220,244]

Scheme 1.8



The important steps are: (I) Co–C bond cleavage (step a) and (II) the rearrangement step of the substrate ($\dot{S}$) to the product ($\dot{P}$) (step c)

(I) Co–C bond cleavage step(a) and organocobaloximes

It is suggested that coenzyme $B_{12}$ acts as an organic radical carrier.[234] Thus, upon mixing a $B_{12}$-dependent enzyme (such as dioldehydrase) with coenzyme, conformational changes take place both in enzyme and coenzyme, which then 'triggers' the Co–C bond cleavage.[71,109,221–233] Unfortunately, no direct information exists on the nature of the conformational changes of the coenzyme. Various possibilities[216,226–231,234] which may contribute to the cleavage include:

(a) Enzyme induced corrin distortion which increases the steric interaction with 5'-adenosyl ligand (5'-Ado);

(b) A change in the position of benzimidazole which induces a corrin distortion as in (a);

(c) A corrin distortion which lengthens the Co–N (benzimidazole) bond;

(d) Direct lengthening or shortening of the Co–C bond; and

(e) Direct lengthening or angular distortion of the Co–C bond.

Of course, combination of effects are also possible. An evaluation of the above possibilities (a–e) with respect to cobaloximes as model is illustrated below.

(a) This effect may be attributed[71,221,222,224,226-231] to a steric cis-influence of the 5'-Ado to the corrin chromophore resulting in a corrin distortion followed by a Co-C bond weakening. This is best illustrated from the structural parameter of $RCo^{III}(dmgH)_2PPh_3$ (1, R = i-Pr; 2, R = 2-butyl). A significantly large Co-C bond and greater distortion of $(dmgH)_2$ ring in (1) compared to (2) leads to a conclusion that packing forces definitely modulate the distortion. That such a lengthening of Co-C bond affects the Co-C bond energy is further evident from the apparent instability of isoproylcobalamin.[231]

(b) The benzimidazole in coenzyme $B_{12}$ lies over six membered chelate rings and the Co-N(3)-C angles are unsymmetrical to avoid contact of the benzimidazole six membered ring with the corrin. Any distortion which moves the benzimidazole over the five membered chelate ring[235] or increases interaction of the benzimidazole six membered ring with corrin can induce a change in corrin pucker which can weaken the Co-C bond by enhancing repulsive interactions between the corrin and the 5'-deoxyadenosine. No crystallographic evidence currently exists for this type of relationship, although the relationship of the orientation of planar L ligands with respect to the size of the equatorial chelate rings has been considered.

(c) The most clear cut relationship between Co-C bond energy and a structural parameter is that between the Co-C bond

strength and the axial Co–N bond length.[225,235] This relationship points out that a lengthening of the Co–N bond by a corrin distortion could also promote Co–C bond cleavage. A good axial donor stabilizes the Co(III) oxidation state and lengthening of the Co–N bond decreases electron donation and destabilizes ($Co^{III}$).[232,233]

(d) If, via interaction of the benzimidazole side chain with the enzyme, the conformational change involves a lengthening of the Co–N bond, the Co–C bond cleavage will be favoured. Conceivably, Co–N bond shortening by a similar process can weaken the Co–C bond by a direct trans influence.[101]

(e) Work with substituted R groups[223–225,236] reveals that the Co–C bond can be stretched easily, which the enzyme may be able to do directly. Rather, large distortion of Co–$C_{\alpha}$–$C_{\beta}$ bond angles have been found in neopentyl cobaloximes[223] whereas neopentyl derivatives of cobalamin are rather unstable.[230,237–24

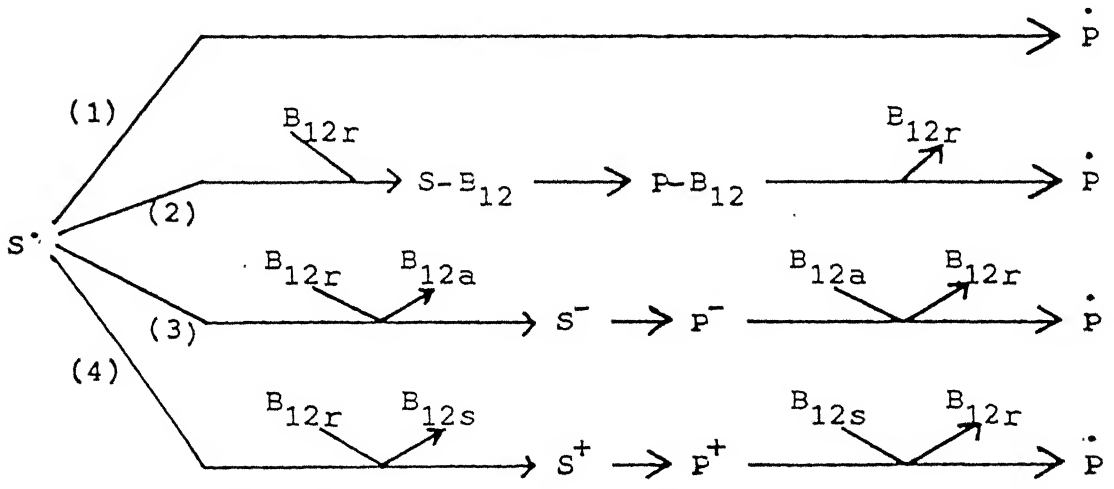
(II) Rearrangement step(c) and organocobaloximes

The least well understood and most controversial aspect of Scheme 1.8[101] is the substrate rearrangement step (c).[240–242] The conversion of the substrate radical $\dot{S}(-\overset{X}{\underset{1}{C}}-\dot{C}_2-)$ to the product radical $\dot{P}(-\dot{\underset{1}{C}}-\overset{X}{\underset{2}{C}}-)$ may follow either free radical or ionic pathways with or without the participation of cobalamin cofactor (Scheme 1.9).[109]

Preliminary proof for (1) has been afforded by Halpern et al. for methylmalonyl Co-A mutase reaction.[243] It is emphasized that the only role of coenzyme $B_{12}$ in these reactions is that of a free radical precursor.

Scheme 1.9.

Alternative pathways for substrate radical rearrangement




$B_{12r}$ = Cob(II)alamin; $B_{12s}$ = Cob(I)alamin.

The alternative mechanism (2) involving the intermediacy of organocobalt adduct has been proposed by many workers on non-enzymatic model studies in a number of $B_{12}$ dependent transformations. The studies carried out by Retey et al.[99,244] and Tada et al.[245,246] on methyl malonylcoenzyme mutase is particularly noteworthy. The role of cobalt moiety has been

attributed to induce steric strain around the migrating group and thus induce rearrangement.[250]

The ionic pathways (3) and (4)[71] lack direct evidence for the intermediacy of the Cob(I) alamin in all $B_{12}$ dependent reactions so far.[82,247-249,251] However, recent studies by Finke et al.[242] on diol dehydrase process are noteworthy. Their model considers a cobalt independent $S^{\ddagger}$ to $P^{\ddagger}$ transformation and also for the first time takes into account the protein bound substrate and coenzyme.

In summary, following understanding from above details can be drawn:

i) Co-C bond is extremely susceptible to facile dissociation conclusively homolytically.[141,233,252]

ii) Steric factors play an important role in weakening the Co-C bond.[253]

iii) Transformation of the substrate is possible, depending totally on the choice of the model system.

iv) Reaction pathways are still open to question and influence of external parameters are still to be understood. However, several reasonable alternatives exist for the nature of conformational change and reaction pathways. More work is required in both model systems and enzymes in order to define the nature of the most important effects.

# CHAPTER-2

## ORGANOCOBALOXIMES: HOMOLYTIC DISPLACEMENT AT SATURATED CARBON CENTRE

### 2.1 Background and Aim of Project

There is a large class of homolytic reactions which result in the net displacement of one radical (or atom) by another radical (or atom).

$$\dot{R} + AB \longrightarrow RA + \dot{B} \qquad .. (A)$$

Such reactions can take place by a number of quite distinct mechanisms, one amongst them is the substitution homolytic, bimolecular reaction referred to as $S_H2$ reaction. In such $S_H2$ reactions the radical $\dot{R}$ attacks a univalent or multivalent centre, however, reactions at tetravalent atoms are relatively rare. Attempts to substitute an asymmetric carbon atom have not led to any firm mechanistic conclusions, though it seems probable that a $S_H2$ reaction at an $Sp^3$ carbon should

$$\dot{X} + RCH_2Y \longrightarrow RCH_2X + \dot{Y} \qquad .. (B)$$

proceed in a manner analogous to $S_N2$ reaction.

A simple molecular orbital energy diagram for the transition state for the symmetrical displacement of $\dot{Y}$ from RY by $\dot{X}$ shows that it is no more forbidden than the corresponding nucleophilic displacement of $Y^-$ by $X^-$ or electrophilic displacement of $Y^+$ by $X^+$, of which there are abundant examples in literature. Since a radical may interact with a filled, a half filled or an empty orbital of the substrate, one might expect the homolytic displacement to be at least as common as its heterolytic counter parts.

One wonders why then such reactions at carbon centre are so seldom postulated and have so frequently been discarded as improbable reactions in the literature ?

One possible answer to this question may be that such homolytic displacement reactions at centres other than carbon like P, S, H, halogens, and addition to unsaturated centres are more common in the systems studied so far.*[254]

Under what circumstances would one expect to observe such reactions at carbon ?

Since the enthalpy change for reaction (B) is simply the difference in enthalpies of dissociation of two bonds i.e. D(C-Y)-D(C-X), the bond formed must be at least as strong as the bond broken.[258] So the first prerequisite is that the

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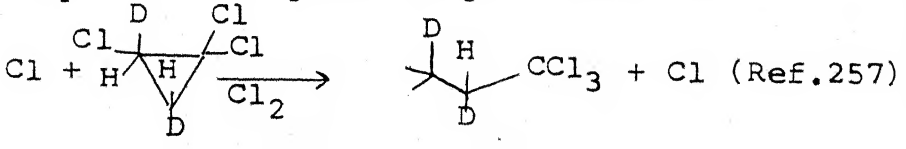
*A few clear exceptions are[255]

$$F_3\dot{C} + Me_4C \longrightarrow F_3CMe + Me_3\dot{C} \quad \text{(Ref. 256)}$$



substrate must have a weak bond between carbon and a suitable homofugal atom or group Y. This condition alone is not sufficient because there are always two ends to any bond and if X-Y is as strong as C-Y bond of the substrate, attack is more likely to occur at Y than at carbon. This is especially so if Y is a univalent atom (H, Cl etc.) or has a relatively unprotected bi-or trivalent element directly attached to the carbon. Therefore, a second prerequisite is that the group Y is not susceptible to attack by X especially at the element bonded to carbon, for example by ensuring that the element is sterically inaccessible.

Organobis(dimethylglyoximato)pyridine cobalt(III), $RCo^{III}(dmgH)_2Py$, trivially known as organocobaloximes, fullfil all the prerequisites and have been employed as good candidates for such a reaction.[150a] The essential feature of these cobaloximes is the low Co-C bond energy which falls within 17-26 kcal/mole and the inorganic radical, cobaloxime(II), $[Co^{II}(dmgH)_2Py]$, so formed by the homolysis of Co-C bond is a good, stable leaving group. It neither disproportionates nor dimerises and can be maintained under anaerobic conditions in certain solvents indefinitely, unlike the majority of the conventional organic radicals.[150a]

Some of the earlier known examples where such a mechanism has been proposed are given below.[92,158,259,26] In these reactions,

the metal for metal exchange reactions are achieved using the inorganic free radicals.

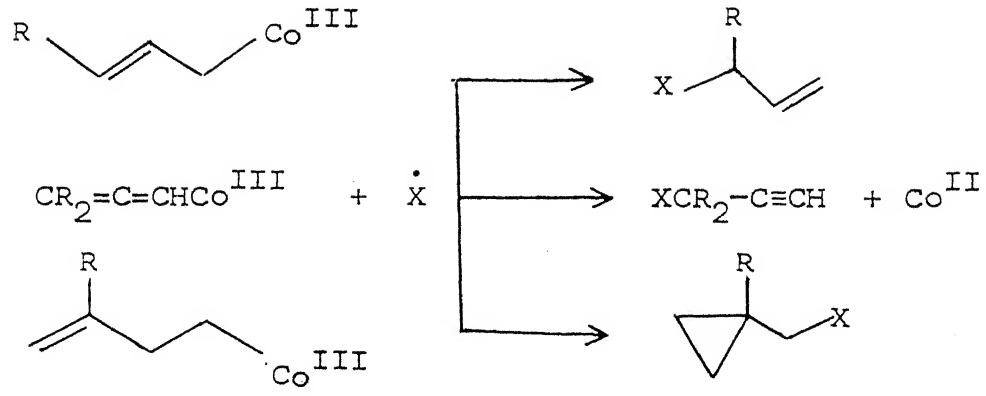
$$RCo^{III}(dmgH)_2Py + Co^{II}(chgH)_2Py \rightleftharpoons RCo^{III}(chgH)_2Py + Co^{II}(dmgH)_2Py$$

$$Cr^{+2}(H_2O)_5 + RCo^{III}(dmgH)_2H_2O \longrightarrow RCr^{III}(H_2O)_5^{2+} + Co^{II}(dmgH)_2H_2O$$

$$SnCl_2 + \text{R-cobalamine(III)} \rightleftharpoons RSnCl_2 + \text{cobalamine(II)}$$

$$Co^{II}(dmgH)_2Py + \text{allyl-}Co^{III}(dmgH)_2Py \rightleftharpoons Py(dmgH)_2CoCH_2\text{-}\dot{C}H\text{-}CH_2Co(dmgH)_2Py \rightleftharpoons Py(dmgH)_2CoCH_2\text{-}CH{=}CH_2 + Co^{II}(dmgH)_2Py$$

More recently, homolytic displacement by conventional organic radicals has been achieved and a number of papers have been published describing the reaction between organocobaloximes and electrophilic free radicals.[150b,174,175,210,211,250,261,262]



X = $CCl_3$, $CBr_3$, $CCl_2CN$, $RSO_2$, $RSO_2NMe$, SPh etc.

Co = $[Co(dmgH)_2Py]$

A chain mechanism is proposed for all these reactions and the key step involved is the homolytic displacement of cobaloxime(II) by attack of the electrophilic free radical at the nucleophilic olefinic carbon of the axial organic group in organocobaloxime forming the regiospecific rearranged organic products*.

Most of the study has been confined to the carbon centred radicals but recently a few S and N centred radicals have also been studied.[174,210,211,262a]

In contrast, all attempts to induce an $S_H2$ displacement at the α carbon of the alkyl chain have proved unsuccessful. However, the study with benzyl cobaloximes has met with partial success,[173] for example homolytic displacement at the benzylic

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* There is only one known example published by our group where prop-2-ynyl and allenyl cobaloximesreact with organosulphonyl chlorides to form the corresponding sulphones by α attack on the axial organic group.[150,254]

carbon has been invoked to account for the formation of ''crossed products'' in the apparent insertion of sulphur dioxide into the C-M bond in a mixture of benzyl cobaloxime and benzyl rhodoximes in liquid sulphur dioxide.[173] We have noticed a similar phenomenon which will be discussed in the third chapter of this thesis.

$$4\text{-}BrC_6H_4CH_2Co(dmgH)_2Py + SO_2 \longrightarrow 4\text{-}BrC_6H_4CH_2SO_2Co(dmgH)_2Py$$
(a) (c)

$$PhCH_2Rh(dmgH)_2Py + SO_2 \longrightarrow PhCH_2SO_2Rh(dmgH)_2Py$$
(b) (d)

$$a + b + SO_2 \longrightarrow c + d + PhCH_2SO_2Co(dmgH)_2Py + 4\text{-}BrC_6H_4CH_2SO_2Rh(dmgH)_2Py$$
(e) (f)

The reactions of benzylcobaloximes with conventional free radicals are rare and only two papers[173a,174a] were noticed before we had undertaken this project. The reactions are not clean and are always accompained by many side reactions.

$$4\text{-}RC_6H_4CH_2Co^{III} \xrightarrow{BrCCl_3} 4\text{-}RC_6H_4CH_2CCl_3 + 4\text{-}RC_6H_4CH_2Br + BrCo^{III}$$

$$4\text{-}RC_6H_4CH_2Co^{III} \xrightarrow{CCl_3SO_2Cl} 4\text{-}RC_6H_4CH_2CCl_3 + (4\text{-}RC_6H_4CH_2)_2 + ClCo^{II}$$

$$PhCH_2Co^{III}(dmgH)_2H_2O + Me_2\dot{C}OH \longrightarrow Me_2C(OH)CH_2Ph + Co^{II}(dmgH)_2H_2O$$

It seems clear that the attack of free radicals on carbon centre is an interesting and useful reaction of great synthetic potential in organic chemistry. However, there is one important aspect of the mechanism that is the subject of contention. Though it seems well established from product, stereochemical, kinetic and thermodynamic studies that the displacement of one paramagnetic metal complex by an identical or near identical complex does proceed through a concerted homolytic displacement reaction, the displacement of a paramagnetic metal complex by a greatly dissimilar organic radical may take place by a two stage process in which an electron transfer is followed by a heterolytic displacement.

$$\dot{X} + R\text{–}M \rightleftharpoons \bar{X}: + R\text{–}M^{+} \rightleftharpoons X\text{–}R + \dot{M}$$

Recently, Espenson et al.[262g,263] have pointed out from their kinetic studies that the direct bimolecular homolytic substitution at the saturated α carbon atom is unlikely and the results are best explained by an addition-elimination mechanism involving one of the oxime ligands or by attack at cobalt. However, benzyl cobaloxime seems to be an exception.

$$\dot{R} + R'Co(dmgH)_2OH_2 \longrightarrow RR' + Co(dmgH)_2H_2O$$

In view of the fact that bimolecular homolytic displacement reactions at the saturated carbon centre by organic free radicals are little studied, we have undertaken the present project where benzyl and parasubstituted benzylcobaloximes and hetero aromatic methyl cobaloximes are reacted with organosulphonyl chlorides. Besides, we believe that the validity of the label $S_H2$ for some of these reactions will remain in doubt until more studies are done in this direction.

Chapter 2 has been divided into two parts. In part 2A reactions of benzyl and parasubstituted benzyl cobaloximes and heteroaromatic methyl cobaloximes with organosulphonyl chlorides are discussed. In part 2B reactions with Mn(III)acetate with these cobaloximes are described.

# CHAPTER - 2A

## REACTIONS OF ORGANOCOBALOXIMES WITH ORGANO SULPHONYL CHLORIDES

## 2.2 Experimental

All reactions were carried out in oven dried (100–120°C) apparatus. Magnetic stirring was provided unless otherwise stated to the reaction procedures. Perfit rotary evaporator was used for concentrating the reaction mixture. Distilled water was used in all aqueous workups.

### Solvents and gases

Commercial grade solvents were used after distillation. 40–60°C, 60–80°C fractions of petroleum ether were commonly used. Chloroform and dichloromethane were distilled from phosphorus pentoxide and kept over molecular seives 4°A type. Methanol and ethanol were distilled from calcium oxide. Benzene, toluene and carbon tetrachloride were kept over calcium chloride and distilled after decantation. Distilled benzene and toluene were kept over sodium wire. Sodium dried diethyl ether and tetrahydrofuran were further distilled from lithium aluminium hydride or calcium hydride prior to use. Tetrahydrofuran was kept over calcium hydride. Pyridine was distilled from potassium hydroxide and stored over potassium hydroxide pellets.

Extra pure IOL AR-2 (impurity 2 ppm) nitrogen was used and purified by passing through traps of Fiser's solution, conc. sulphuric acid and potassium hydroxide pellets. Oxygen gas was used directly from the cylinder.

Chromatography

Small plates suitable for preliminary exploration of the chromatographic process with regard to the selection of solvent for preparative chromaplate or for monitoring reaction process were prepared from microscopic slide using Merck Silica gel-G. For preparative chromaplate silica gel-G or alumina (neutral) were used. Flash column chromatography was often used using silica gel-G and handy aspirator. Visualization of spots or bands were effected by expsure to iodine vapour generally.

Gas liquid chromatography was employed for the rapid convenient analysis of the composition of mixture of organic compounds (comparing with authentic samples) on Shimadzu Chromatograph GC-9A using SE-30 column.

Iatroscan TH-10 was used for getting the ratios of the organic product mixture.

Physical measurements and instruments used

Melting points (m.p.) were determined on Fisher-Johns and perfit melting point apparatus and are uncorrected. Boiling points (b.p.) are also uncorrected.

Infrared (IR) spectra were recorded on Perkin-Elmer model 3220 and 850 infrared-grating spectrophotometers and are reported in wave numbers ($cm^{-1}$). Electronic spectra were recorded on Cary-17D and Shimadzu UV-190 double beam spectrophotometers. Proton magnetic resonance ($^1H$ NMR) spectra were recorded on 400 MHz (Bruker WH-400), 90 and 100 MHz (Varian EM-390 and HA-100) spectrometers. Chemical shifts are reported in ppm downfield from internal reference TMS ($\delta$). Multiplicity is indicated using following abbreviations: s (singlet), d (doublet), t (triplet), q (quarter), m (multiplet), br (broad), etc. Coupling constants are reported wherever necessary and are expressed in Hertz (Hz).

Mass spectra were recorded at Regional Sophisticated Instrument Centre, Lucknow on VG Micromass 7070F mass spectrometer. Principal molecular fragments are reported.

Carbon, hydrogen and nitrogen analyses were carried out at Central Microanalytical Lab., I.I.T. Kanpur and Regional Sophisticated Instruments Centre (CDRI), Lucknow.

Starting Materials

Benzyl chloride, 4-chlorobenzyl chloride, dibenzoyl peroxide, bromobenzene, bromine, 4-cresol, dimethylsulphate, lithium aluminium hydride, 4-nitrotoluene, para-formaldehyde, phosphorus pentachloride, pyridine, red-phosphorus, sodium borohydride, sodium hydride, sulphuryl chloride, thionyl chloride, 4-tolualdehyde, 4-toluonitrile, tosyl chloride, meta- and para-xylene, methane sulphonyl chloride, 2,4,5-trichlorobenzene-sulphonyl chloride, chlorosulphonic acid, thiophene, 3-methyl-thiophene, furfuryl alcohol, propargyl alcohol, p-toluene sulphonic acid, phosphorous tribromide, sodium hydride (60% oil suspension), N-bromosuccnimide, cobalt(II) chloride hexahydrate, dimethylglyoxime, 4-methoxybenzyl bromide, 2-(bromomethyl) naphthalene were commercial materials (mostly Aldrich) and in general were either distilled or recrystallized before use.

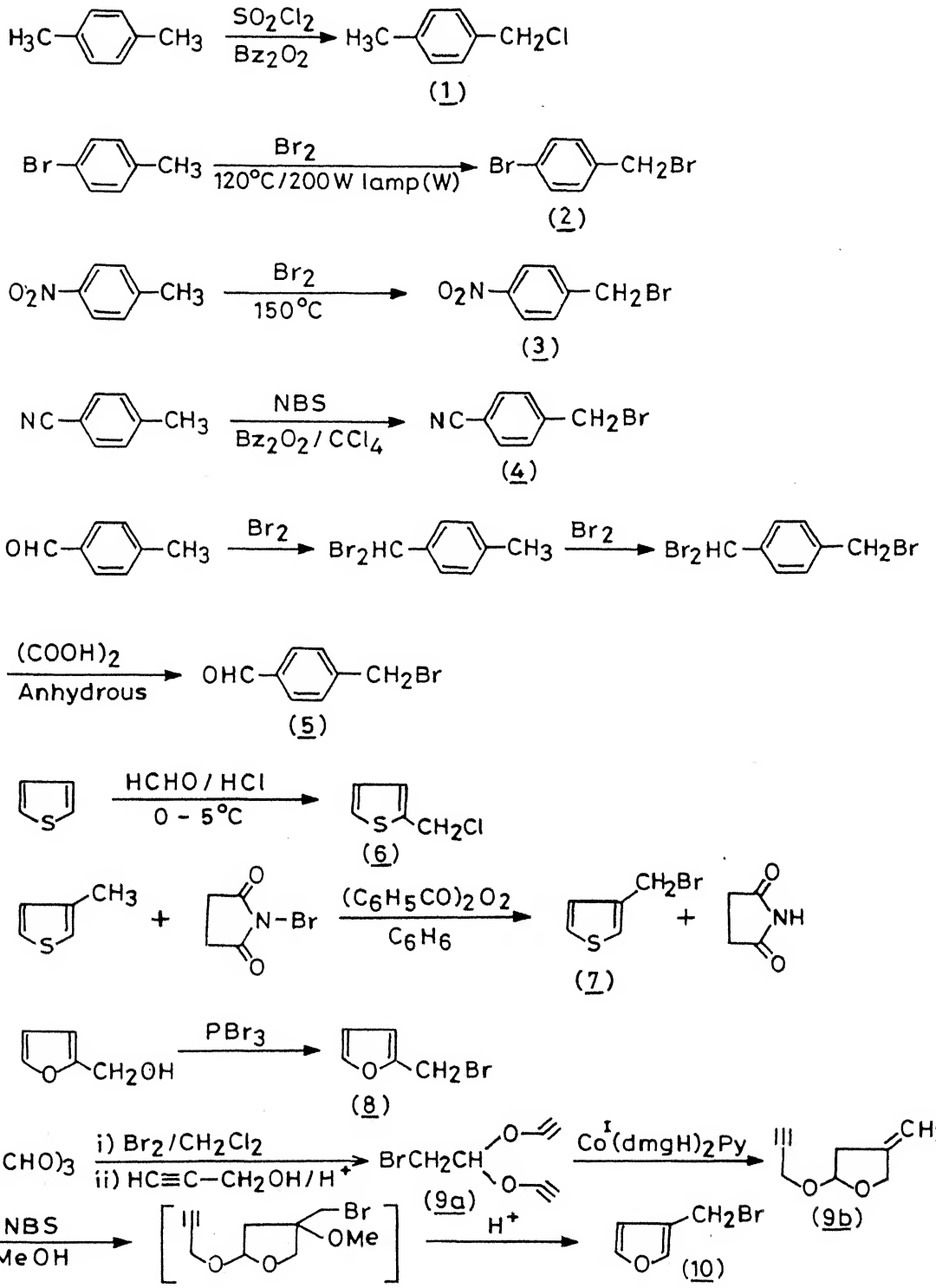
## 2.2.1 Synthesis of Organic Precursors

The preparative routes for organic precursors are outlined in scheme (2.1), described below.

Preparation of 4-methyl benzyl chloride(1)[264]

A mixture of p-xylene (10.0 g), sulphuryl chloride (9.0 g) and dibenzoyl peroxide (0.05 g) in dry carbon tetrachloride (25 ml) was heated to reflux for two hr. Excess p-xylene and carbon

## Scheme 2.1


H3C—CH3
SO2Cl2
Bz2O2
H3C—CH2Cl
(1)
Br—CH3
Br2
120°C/200W lamp(W)
Br—CH2Br
(2)
O2N—CH3
Br2
150°C
O2N—CH2Br
(3)
NC—CH3
NBS
Bz2O2/CCl4
NC—CH2Br
(4)
OHC—CH3
Br2
Br2HC—CH3
Br2
Br2HC—CH2Br
(COOH)2
Anhydrous
OHC—CH2Br
(5)
HCHO/HCl
0 - 5°C
CH2Cl
(6)
CH3
N-Br
(C6H5CO)2O2
C6H6
CH2Br
NH
(7)
CH2OH
PBr3
CH2Br
(8)
(CH3CHO)3
i) Br2/CH2Cl2
ii) HC≡C—CH2OH/H+
BrCH2CH
(9a)
Co^I(dmgH)2Py
CH2
(9b)
NBS
MeOH
Br
OMe
H+
CH2Br
(10)

tetrachloride were removed and the residue was distilled to give 4-methyl benzyl chloride (10.5 g, 79%), b.p. 67°/5 mm (lit.[264] b.p. 92°/20 mm).

$^1$H NMR ($CDCl_3$), δ (ppm): 7.28-6.95 (m, Ph), 4.48 (s, $-CH_2$), 2.31 (s, $CH_3$).

Preparation of 4-bromobenzyl bromide (2)[265]

Bromine (10.2 g) was added dropwise during 30 minutes with irradiation to 4-bromotoluene (10.2 g) at 120°C. Stirring was continued for two hr. The product which got solidified on cooling was filtered and washed with ethanol (3 x 10 ml). The product was recrystallized using light petroleum ether:benzene (80:20) mixture. Yield (9.8 g, 65%); m.p. 60°C (lit.[265] m.p. 61°C).

$^1$H NMR ($CDCl_3$), δ (ppm): 7.1-7.5 (m, Ph), 4.38 (s, $-CH_2$).

Preparation of 4-nitrobenzyl bromide (3)[266]

Bromine (36.8 g) was added dropwise during two hr. to 4-nitrotoluene (30.0 g) at 150°C. Reaction mixture was poured into petroleum ether (60-80°C) (400 ml). The crude product was recrystallized using benzene:petroleum ether mixture (50:50). Yield (22.0 g, 88%); m.p. 96°C (lit.[266] m.p. 97.5-99.0°C).

$^1$H NMR ($CDCl_3$), δ (ppm): 7.35-8.20 (m, Ph), 4.5 (s, $-CH_2$).

Preparation of 4-cyanobenzyl bromide (4)[267]

4-Toluonitrile (14.6 g, in 50 ml carbon tetrachloride) was added dropwise to a suspension of N-bromosuccinimide (18.0 g, in 50 ml carbon tetrachloride) and dibenzoyl peroxide (0.3 g). Reaction mixture was heated to reflux for two hr. The solution was filtered hot and the filtrate was evaporated to half its volume. Crude product was recrystallized from ethanol (14.0 g, 80%), m.p. 114°C (lit.[267] m.p. 116°C).

$^1$H NMR ($CDCl_3$), δ (ppm): 7.5-7.8 (m, Ph), 4.52 (s, $-CH_2$).

Preparation of 4-bromomethyl benzal dehyde (5)[268]

Bromine (25 ml) was added dropwise to red-phosphorus (6.2 g) in carbondisulphide (60 ml) with cooling followed by 4-tolualdehyde (16.0 g). The mixture was heated to reflux for two hr. On cooling, water (100 ml) was added, carbon disulphide layer was separated, washed with water, and dried over calcium carbonate. Carbon disulphide layer was distilled off and the crude product, 4-methyl benzil bromide, thus obtained was purified using ethanol and active charcol (12.0 g, 60%). m.p. 62°C (lit.[268] m.p. 62°C). This was further brominated at 140°C with uv irradiation giving W,W,W'-tribromoparaxylene (10.9 g, 70%), m.p. 104°C (lit.[268] m.p. 106°C). Dry oxalic acid (2.5 g) was added in small portion to W,W,W'-tribromoparaxylene (5.7 g) at 150-160°C. Reaction mixture was further heated for 1.5 hr. On

cooling, the reaction mixture was extracted with ethanol and crude product was purified using ethanol-water and active charcol. The product was recrystallized using petroleum ether (3.0 g, 72 ), m.p. 92°C (lit.[268] m.p. 95.3°C).

$^1$H NMR ($CDCl_3$), δ (ppm): 6.95-8.0 (m, Ph), 4.52 (s, $-CH_2$), 9.8 (s, CH).

## Preparation of 2-chloromethylthiophene (6)[269]

A rapid stream of dry hydrogen chloride was passed into a stirred mixture of thiophene (21.0 g) and conc. hydrochloric acid (10 ml) at 0°C. 40% Formaldehyde solution (25 ml) was added dropwise maintaining the temperature at 0-5°C after which, the mixture was extracted with ether (3 x 25 ml). The ether solution was successively washed with water, saturated sodium bicarbonate solution and water, then dried over anhydrous calcium chloride. Removal of solvent and distillation under reduced pressure gave the product (6) as yellow oil, (10.0 g, 30%), b.p. 67-68°/10 mm (lit.[269] b.p. 73-77°/17 mm).

## Preparation of 3-bromomethylthiophene (7)[270]

A mixture of N-bromosuccinimide (18.0 g) and dibenzoyl

peroxide (0.2 g) was added to a refluxing solution of 3-methylthiophene (11.0 g) in dry benzene (40 ml). The mixture was immediately cooled and succinimide filtered. Removal of solvent at reduced pressure and fractional distillation of residue gave 3-bromomethylthiophene (7) (10.0 g; 51%), b.p. 76°/1 mm (lit.[270] b.p. 75-78°/1 mm).

Preparation of furfuryl bromide (8) in ether solution[271]

A solution of phosphorous tribromide (5.0 g) in dry ether (10 ml) was added dropwise to a mixture of furfuryl alcohol (5.0 g) in dry ether (40 ml) at 5-10°C. The mixture was brought to room temperature and the ether solution was decanted off. Treatment first with 50%KOH solution and then with solid KOH gave a pale yellow ether solution of furfuryl bromide (8) which was used directly for the next step.

Preparation of 2,2-bis(propynyloxy)ethyl bromide (9a)[272]

A solution of bromine (15 ml) in dichloromethane (50 ml) was added dropwise to a stirred mixture of paraldehyde (12.5 ml) and flame dried magnesium sulphate (2.0 g) in dichloromethane

(25 ml) at 5-10°C. Stirring was continued at room temperature until all the bromine was decolorised and no more HBr escaped from the solution. After filtration the solution was heated successively with solid sodium thiosulphate and solid sodium bicarbonate till it was neutral. It was then dried over anhydrous magnesium sulphate, filtered and again kept over flame dried magnesium sulphate. A mixture of propargyl alcohol (24.0 g, 25 ml) and p-toluene sulphonic acid (1.5 g) was slowly added to the solution at room temperature when the colour changed from yellow to violet. After stirring for further two hr., the mixture was filtered and solvent removed at room temperature in vacuo. The residue was treated with water and extracted with 3 x 50 ml ether. The ether solution was washed with saturated sodium bicarbonate solution, brine solution and dried over anhydrous magnesium sulphate. Solvent removal in vacuo and distillation under reduced pressure afforded 2,2-bis(propynyloxy)ethyl bromide (9a) (42 g; 90%), b.p. 84-92°/1-2 mm.

$^1$H NMR ($CCl_4$) δ(ppm): 2.50 (t, 2H, J=2 Hz), 3.40 (d, 2H, J=5 Hz), 4.28 (d, 4H, J=2 Hz), 5.00 (t, 1H, J=5 Hz).

Preparation of 2-(2-propynyloxy)-4-methylenetetrahydrofuran (9b)[272]

Chlorocobaloxime (6.0 g) was added under nitrogen atmosphere to a solution containing sodium borohydride (7.5 g), sodium hydroxide (6.0 g in 25 ml water) and pyridine (75 ml) in ethyl alcohol (600 ml). To the dark blue solution of cobalt(I) was added dropwise a solution of bromide (9a) (32.4 g, 23 ml) in ether (150 ml) over a period of 4 hr. under water cooling. After removal of the solvent at 40°C under reduced pressure, 250 ml of brine was added and the mixture was extracted with ether:hexane (1:1) (10 x 75 ml). The combined extracts were washed with brine and dried over anhydrous sodium sulphate. Solvent removal in vacuo and distillation gave 2-(2-propynyloxy)-4-methylenetetrahydrofuran (9b); yield 9.2 g (44%), b.p. 62-65°/10 mm (lit.[272] b.p. 73-76°/18 mm).

$^1$H NMR ($CCl_4$) δ(ppm): 2.40 (t, 1H, J=2 Hz), 2.45-2.7 (m, 2H), 4.15 (d, 2H, J=2 Hz), 4.25-4.40 (m, 2H), 4.8-5.0 (m, 2H).

Preparation of 3-(bromomethyl)furan (10)[272]

A mixture of (9b) (4.1 g; 30 mmol) and N-bromosuccinimide (6.4 g; 36 mmol) in methanol (50 ml) was stirred at room temperature overnight. Methanol was evaporated at room temperature in vacuo and ether (50 ml) was added to the residue. The ether layer was washed with 1N-sodium hydroxide solution, dried

over anhydrous sodium sulphate and concentrated to give crude 1-bromo-2,2-di(propynyloxy)ethane. Dry benzene (50 ml) and p-toluene sulphonic acid were added to the residue and the mixture was refluxed for two hr. after which it was extracted with ether (3 x 50 ml). The ether layer was washed with aqueous sodium bicarbonate solution and dried over anhydrous magnesium sulphate. Solvent removal and fractional distillation gave 3-furyl bromide (10) yield. 2.6 g (54%), b.p. 49-50°/10 mm (lit.[272] b.p. 62-64°/25 mm).

$^1$H NMR ($CCl_4$) δ(ppm): 4.40 (s, 2H), 6.35 (s, 1H), 7.33 (t, 1H) and 7.50 (m, 1H).

Preparation of benzene sulphonyl chloride ($A_1$)[266]

Sodium benzene sulphonate (9.0 g) and powdered phosphorous pentachloride (5.0 g) were placed in a R.B. flask furnished with a reflux condenser. The mixture was heated for 12-15 hr. at 170-180°C. Every 3 hr., the flask was removed from the oil bath and allowed to cool, then shaken thoroughly until the mass becomes pasty. At the end of the heating period the reaction mixture was allowed to cool and poured into crushed ice, extracted the crude benzene sulphonyl chloride with 15 ml of carbon tetrachloride and the aqueous layer with 8 ml of the same solvent. After removal of the solvent and distillation gave benzene sulphonyl chloride ($A_1$). Yield 6.2 g (75%), b.p. 96°/5 mm (lit.[266] b.p. 118-120°/15 mm).

## Preparation of 4-methyl benzene sulphonyl chloride ($A_2$)[266]

Chlorosulphonic acid (22.8 ml) was placed in a flask and cooled to 0°C. Pure and dry toluene (11.5 ml) was added dropwise with stirring at such a rate that the temperature of the mixture did not rise above 5°C. After addition of all the toluene, the reaction mixture was stirred for 4 hr. and then allowed to stand over night in the freezing mixture. The liquid was poured into crushed ice and the aqueous solution from the oily layer was separated and washed the latter several times by decantation with cold water. The oil was cooled at -10° to -20°C for several hrs. The almost pure 4-methyl benzene sulphonyl chloride crystallized out. It was filtered at the pump and dried. The product was recrystallized from petroleium ether (40-60°). Yield 63%, m.p. 68° (lit.[266], 69°).

## Preparation of 4-methoxy benzene sulphonyl chloride ($A_3$)

This compound was prepared by the method described above using 10.8 ml anisole and 19.5 ml chlorosulphonic acid. Yield 59%; m.p. 41° (lit.[266] 42°).

## Preparation of 4-chlorobenzene sulphonyl chloride ($A_4$)

Compound ($A_4$) was prepared by the method described above using 11.2 ml chlorobenzene and 19.5 ml chlorosulphonic acid. Yield 51%; m.p. 51° (lit.[266] 51°).

Preparation of 4-bromobenzene sulphonyl chloride ($\underline{A}_5$)

Using 15.7 ml bromobenzene and 19.5 ml chlorosulphonic acid compound ($\underline{A}_5$) was prepared by the same method described above. Yield 49%, m.p. 75° (lit.[266] 75°).

## 2.2.2 Synthesis of Cobaloximes

The preparative routes for the cobaloximes are outlined in scheme 2.2 and prepared by the methods[37] described below:

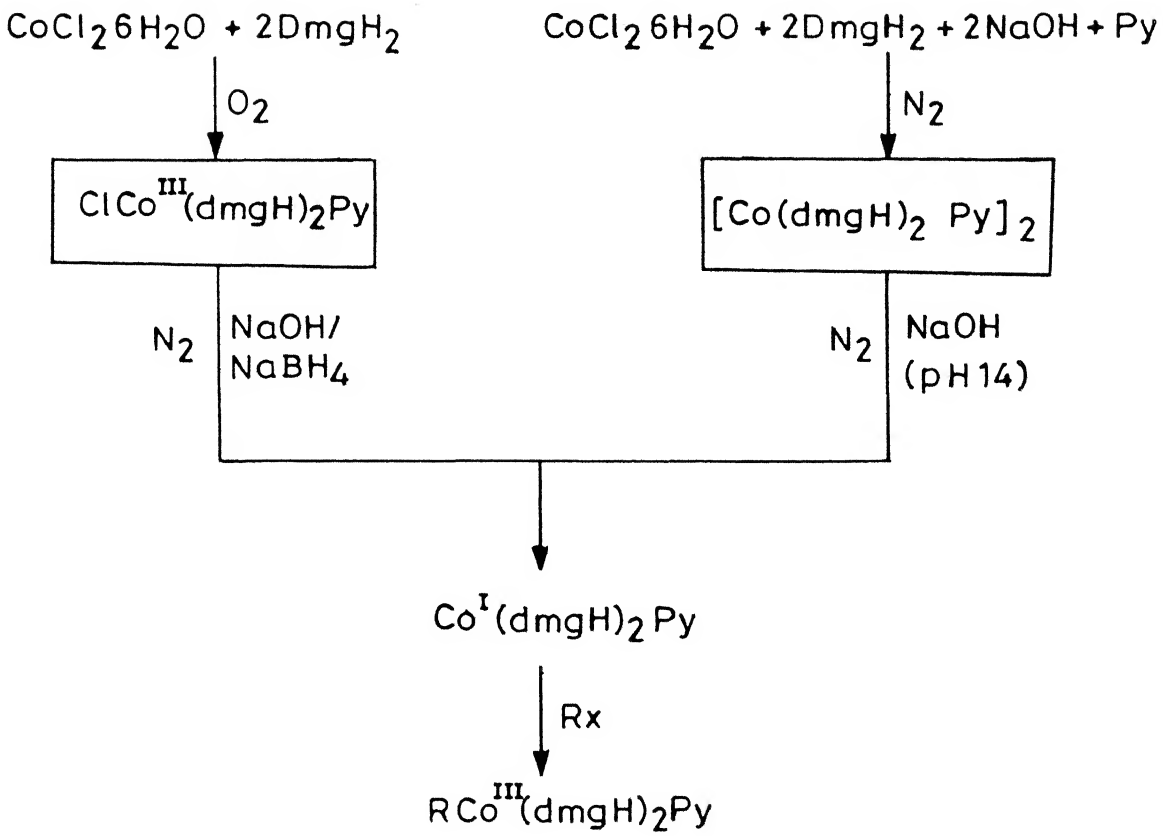
METHOD S.1

Chloro(pyridine)cobaloxime(III) (11)[37]

Pyridine (3.6 g) was added to a hot solution of cobalt(II) chloride hexahydrate (5.0 g, 21 mmol) and dimethylglyoxime (5.5 g, 47 mmol) in 95% ethanol (200 ml). After cooling to room temperature a stream of air was blown through the solution for 0.5 hr. The product (11) was allowed to crystallize out from solution, which was filtered, washed successively with water, ethanol and ether and dried at room temperature in vacuo, (5.0 g, 58% based on cobalt(II) chloride hexahydrate).

$^1$H NMR ($CDCl_3$), δ(ppm): 2.35 (s, $CH_3$), [8.25 (γ, d, Py), 7.26 (α, m, Py), 7.73 (β, m, Py)]

## Scheme 2.2

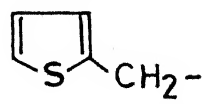
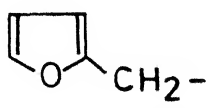


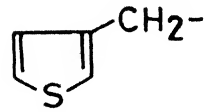
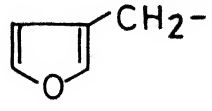

R = (12) $C_6H_5CH_2-$, (13) 4-$CH_3C_6H_4CH_2-$

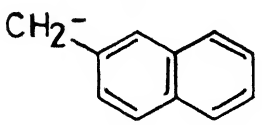
(14) 4Br$C_6H_4CH_2-$, (15) 4-Cl$C_6H_4CH_2-$

(16) 4-$CNC_6H_4CH_2-$ (17) 4-$NO_2C_6H_4CH_2-$

(18) 4-$CHOC_6H_4CH_2-$ (19) 4-OMe $C_6H_4CH_2-$

(20)  (21) 

(22)  (23) 

(24) 

METHOD S.2

Preparation of benzyl (12), 4-methylbenzyl (13), 4-bromobenzyl (14), 4-chlorobenzyl (15), 4-cyanobenzyl (16), 4-nitrobenzyl (17), 4-formylbenzyl (18), 2-thienylmethyl (20), 3-thienylmethyl (22) and naphthyl (24) cobaloximes

A mixture of cobalt(II) chloride hexahydrate (9.52 g, 40 mmol) and dimethylglyoxime (9.38 g, 80 mmol) were stirred in methanol (200 ml) in a 500 ml three-necked R.B. flask fitted with a gas inlet tube, a pressure equalising dropping funnel and an adapter outlet connected to a mercury trap. A stream of pure, dry nitrogen was passed through the mixture for 30 minutes. An aqueous solution of sodium hydroxide (Ca. 5-6 ml, 80 mmol) was added to the mixture followed by pyridine (2.2 ml, 40 mmol). The mixture was cooled in an ice-salt bath and aqueous sodium hydroxide (Ca. 6-8 ml, 100 mmol) was added. A deep-blue solution was formed. Appropriate organic halide (40 mmol) in methanol (10 ml) was added dropwise to the mixture. The colour changed from blue to red. The solution was stirred for another 3 hr. and brought to ambient temperature. Approximately one-third volume of solvent was evaporated under reduced pressure and the mixture was poured into water (200 ml) containing few drops of pyridine. The precipitated solid was washed with cold water (Ca. 300 ml) until the washings were pale yellow. It was then washed with ether (Ca. 3 x 25 ml) and dried in vacuo. An analytical sample was

obtained by recrystallizing the product from hot 50% aq. ethanol which was yellow to orange in colour.

METHOD S.3

Preparation of furfuryl (21), 3-furylmethyl (23) and 4-methoxy benzyl (19) cobaloximes

To a suspension of chlorocobaloxime (11) (20 mmol) in methanol (150 ml) was added, under nitrogen, a few drops of aqueous sodium hydroxide followed by solid sodium borohydride (40 mmol). To the resulting deep blue solution, 3-furyl bromide (10) or 4-methoxybenzyl bromide in methanol (10 ml) was added dropwise. However, for furfuryl bromide (8), its etheral solution was used for addition. The workup procedure was same as described in method above.

### 2.2.3 Reaction of organocobaloximes (12 to 17, 20 to 23) with organosulphonyl chlorides ($A_1$-$A_6$)

The reactions have been carried out by the following general methods:

#### Under Thermal Conditions (T)

A stream of nitrogen gas was passed for 15 minutes through dichloromethane (30 ml) taken in a 50 ml two-necked R.B. flask. Organocobaloxime (2 mmol), organosulphonyl chloride (2.5 mmol) were added successively. The mixture was heated to reflux on a water bath under a positive pressure of nitrogen. The reaction was monitored by TLC on silica gel using ethyl acetate as eluent.

After completion of the reaction, the mixture was concentrated in vacuo and subjected directly to flash chromatography using dichloromethane as eluent. The unreacted sulphonyl chloride was eluted first followed by the organic product. The eluent was then changed to dichloromethane:acetone mixture (1:4) when the inorganic product was eluted out. The crude organic product thus obtained was further purified by preparative TLC using chloroform:petroleium ether (60-80°C) mixture (3:1, v/v) as eluent. Solid products were further recrystallised from petroleiumether (40-60°C): chloroform mixture (4:1, v/v) as white solids.

#### Under photochemical conditions

a) Using 2 x 200 Watt Tungsten Lamps (P.1)

Organocobaloxime (2 mmol) and organosulphonyl chloride

(2.5 mmol) were added successively to degassed dichloromethane (50 ml). The reaction was carried out in a specially designed glass apparatus attached to Julabo refrigerated circulator (UC-20 model). Two 200 W tungsten lamps were placed 5 cm apart from the reaction vessel and the solution at 0°C was irradiated. The reaction was monitored for cobaloxime by TLC on silica gel using ethyl acetate as eluent.

After completion of the reaction the mixture was concentrated in vacuo and subjected directly to flash chromatography using dichloromethane as eluent and was worked up as described under thermal condition (method T).

b) Using Srinivasan's Photoreactor* (400 W Mercury lamp) (P.2)

A solution of organocobaloxime (2 mmol), 4-methyl benzene sulphonyl chloride (2.5 mmol) in dry chloroform (45 ml) was thoroughly degassed with nitrogen for 15 minutes. The mixture was transfered into quartz tubes (15 ml capacity), under nitrogen and stoppered. The tubes were placed in the reactor and irradiated by a 400 W mercury lamp placed inside a double walled quartz tube, through which ice-cold water was circulated maintaining the temperature at 25°C. The reaction mixture was work up as detailed under method T earlier.

---

* 400 Watt mercury lamp (medium pressure) emit radiations predominantly at 365-366 nm with smaller amounts in UV region at 297, 303, 313 and 334 as well as significant amounts in the visible region at 404-408, 436, 546 and 577-579 nm.

In the presence of dibenzoyl peroxide/galvinoxyl

Dibenzoyl peroxide/galvinoxyl (Ca. 5% , w/w) was added to 30 ml dichloromethane containing organocobaloxime (2 mmol), 4-methylbenzenesulphonyl chloride (2.5 mmol) and pyridine (5 drops) and the reaction was carried out as described under method T.

## 2.3 Results and Discussion

### 2.3.1 Formation of organocobaloximes (12-24)

Benzyl (12-19), heteroaromatic methyl (20-23) and naphthyl cobaloximes (24) are prepared by reacting the appropriate halide with preformed ($Co^{I}$), the latter being generated either by the reduction of chloro cobaloximes by sodium borohydride in alkaline medium or by the disproportionation of ($Co^{II}$) dimer into ($Co^{III}$) and ($Co^{I}$) in highly alkaline medium.[170,273,274] The reaction of ($Co^{I}$) with halides are visibly fast (only on the basis of colour change from blue ($Co^{I}$) to red ($Co^{III}$) . The organocobaloximes have been isolated by standard work-ups in all cases except for 4-nitrobenzyl cobaloxime (17) which readily decomposes in solution and is therefore worked-up just after the addition of halides.

Although the electron transfer mechanism has recently been invoked for many cobaloximes, however in the present case

Table 2.1. Spectral Characteristic of Organocobaloximes, $RCo^{III}(dmgH)_2Py$, (11-24)

| Compound No. | R | $^1H$ NMR Chemical shift(δ): ($CDCl_3$) (ppm), (TMS) | | | | | | Others | UV-vis: $\lambda_{max}$ (nm (log ε) ($CH_3$ |
|---|---|---|---|---|---|---|---|---|---|
| | | dmgH | $CH_2$ | Aromatic | Pyridine | | | | |
| | | | | | α | β | γ | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| (11) | Cl | 2.35 | - | - | 7.26 | 7.73 | 8.25 | - | 468, 360, 275, 233 |
| (12) | $C_6H_5CH_2$ | 1.90 | 2.80 | 6.95 | 7.32 | 7.73 | 8.40 | - | 455, 352, 272, 238 |
| (13) | 4-$MeC_6H_4CH_2$ | 1.95 | 2.90 | 6.90 | 7.36 | 7.78 | 8.52 | 2.08(Me) | 452, 356, 274, 237 |
| (14) | 4-$BrC_6H_4CH_2$ | 1.98 | 2.82 | 7.00-7.45 | 7.40 | 7.90 | 8.56 | - | 421, 347, 262, 227 |
| (15) | 4-$ClC_6H_4CH_2$ | 2.00 | 2.73 | 7.20 | 7.30 | 7.80 | 8.56 | - | 455, 353, 270, 240 |
| (16) | 4-$CNC_6H_4CH_2$ | 1.98 | 2.71 | 6.90-7.30 | 7.25 | 7.70 | 8.50 | - | 460, 340, 277, 237 |
| (17) | 4-$NO_2C_6H_4CH_2$ | 2.06 | 3.35 | 6.86-7.54 | 7.72 | 8.22 | 8.76 | - | 445, 350, 300, 235 |

...contd.

Table 2.1(contd.)

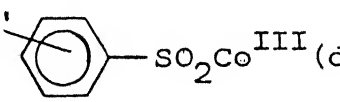
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| (18) | 4-$CHOC_6H_4CH_2$ | 1.96 | 2.78 | 6.98-7.40 | 7.30 | 7.65 | 8.52 | 9.86(CHO) | 458,342, 277,238 |
| (19) | 4-$MeOC_6H_4CH_2$ | 1.95 | 2.85 | 6.60-6.90 | 7.25 | 7.68 | 8.55 | 3.75(OMe) | 448,380, 287,232 |
| (20) | 2-Thienyl-methyl | 2.05 | 3.00 | 6.65 7.00 | 7.20 | 7.65 | 8.50 | | 385(3.42) 281(3.12) 240(3.49) |
| (21) | Furfuryl | 2.00 | 2.40 | 6.00 7.40 | 7.30 | 7.75 | 8.60 | | 383(3.39) 284(3.18) 239(3.58) |
| (22) | 3-Thienyl-methyl | 2.00 2.10 | 2.85 | 6.65 7.20 | 7.30 | 7.70 | 8.50 | | 359(3.20) 277(3.21) 239(3.60) |
| (23) | 3-Furyl-methyl | 2.00 2.10 | 2.55 | 6.00 7.12 | 7.15 | 7.75 | 8.42 | | 348(3.22) 286(3.31) 238(3.56) |
| (24) | Naphthyl | 1.70 | 2.13 | 6.98-7.71 | a | a | 8.33 | | 325,289, 278,268 |

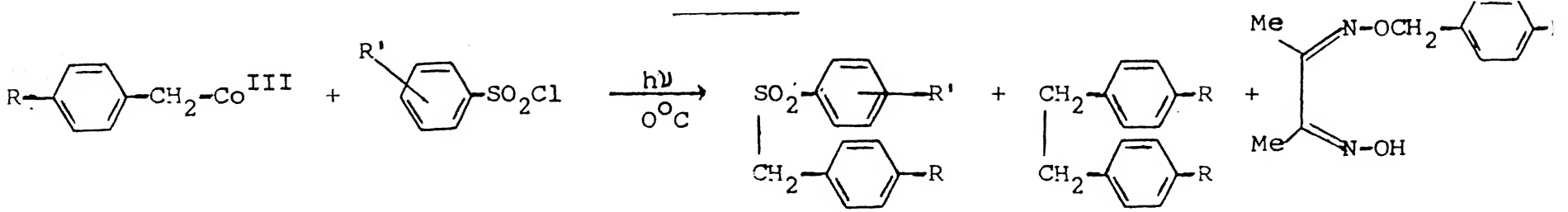
All compounds give satisfactory C,H, and N analyses.

a, obscured.

the mechanism for the formation of cobaloximes may follow $S_N2$ displacement of the halide ion by ($Co^I$) nucleophile. The spectral characteristics of the cobaloximes (12–24) are listed in Table 2.1.

### 2.3.2 Reaction of organo cobaloximes (12–17) and (20–23) with benzenesulphonyl chlorides ($A_1$–$A_6$)

4–Chlorobenzenesulphonyl chloride ($A_4$) reacts with 4–methylbenzyl cobaloxime (13) in 1:1 molar ratio in dichloromethane at $0^oC$ under anaerobic and photolytic conditions. A smooth reaction takes place and is complete within 2 hr. to give the sulphone (32) in 37% yield. The reaction is, however, subject to induction period, the length of which depends upon the purity of the substrate cobaloxime. The rate of reaction is lowered by added galvinoxyl and is accelerated by dibenzoyl peroxide. Similar reactions of benzylcobaloximes (12–17) with 4–methyl–, 4–chloro–, 4–bromo–, 4–methoxy, 2,4,5–trichlorobenzenesulphonyl chlorides ($A_2$–$A_6$) under identical conditions form benzylsulphones (25–54) in 8–66% yield. All the reactions are accompained by bibenzyls (55–60) in variable yields. Benzyldimethylglyoxime monoethers, 4–R–$C_6H_4CH_2$–ON=CMe–CMe=NOH (61–66) are found as side products in certain cases (see table). $ClCo^{III}$–$(dmgH)_2Py$ and  ($SO_2Co^{III}(dmgH)_2Py$ (R'=Me, OMe, Cl, Br, 2,4,5,$Cl_3$) are the inorganic cobaloximes isolated in all cases.




| | | | | |
|---|---|---|---|---|
| (12) R=H | ($A_2$) R'=4-Me | (25) R=H; R'=4-Me | (55) R=H | (61) R=H |
| | ($A_3$) R'=4-OMe | (26) R=H; R'=4-OMe | " | - |
| | ($A_4$) R'=4-Cl | (27) R=H; R'=4-Cl | " | - |
| | ($A_5$) R'=4-Br | (28) R=H; R'=4-Br | " | R=H |
| | ($A_6$) R'=2,4,5 $Cl_3$ | (29) R=H; R'=2,4,5 $Cl_3$ | " | - |
| (13) R=Me | | (30) R=Me; R'=4-Me | (56) R=Me | (62) R=Me |
| | | (31) R=Me; R'=4-OMe | " | - |
| | | (32) R=Me; R'=4-Cl | " | R=Me |
| | | (33) R=Me; R'=4-Br | " | R=Me |
| | | (34) R=Me; R'=2,4,5 $Cl_3$ | " | - |
| (14) R=Br | | (35) R=Br; R'=4-Me | (57) R=Br | (63) R=Br |
| | | (36) R=Br; R'=4-OMe | " | R=Br |
| | | (37) R=Br; R'=4-Cl | " | - |
| | | (38) R=Br; R'=4-Br | " | - |
| | | (39) R=Br; R'=2,4,5 $Cl_3$ | " | - |

...contd.

| | | | |
|---|---|---|---|
| (15) R=Cl | (40) R=Cl; R'=4-Me | (58) R=Cl | - |
| | (41) R=Cl; R'=4-OMe | " | - |
| | (42) R=Cl; R'=4-Cl | " | (64) R=Cl |
| | (43) R=Cl; R'=4-Br | " | R=Cl |
| | (44) R=Cl; R'=2,4,5 $Cl_3$ | " | - |
| (16) R=CN | (45) R=CN; R'=4-Me | (59) R=CN | (65) R=CN |
| | (46) R=CN; R'=4-Me | " | " |
| | (47) R=CN; R'=4-Cl | " | " |
| | (48) R=CN; R'=4-Br | " | " |
| | (49) R=CN; R'=2,4,5 $Cl_3$ | " | " |
| (17) R=$NO_2$ | (50) R=$NO_2$; R'=4-Me | (60) R=$NO_2$ | (66) R=$NO_2$ |
| | (51) R=$NO_2$; R'=4-OMe | " | " |
| | (52) R=$NO_2$; R'=4-Cl | " | " |
| | (53) R=$NO_2$; R'=4-Br | " | " |
| | (54) R=$NO_2$; R'=2,4,5 $Cl_3$ | " | " |

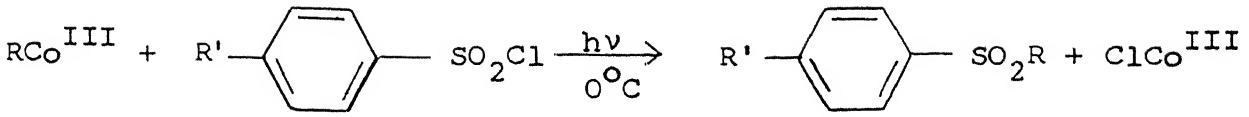
When the reactions are carried out in the presence of one mol excess of pyridine, the yields of the sulphones are improved by ≃20% in each case and the amount of bibenzyls decreased with no trace of the formation of mono ethers. The reactions take much longer time under thermal conditions and the yields of sulphones are much lower to those obtained under photolytic conditions. The characteristics of all the organic products are given in scheme 2.3 and table 2.2 to 2.4 and 2.6.

On the other hand, heteroaromatic methyl cobaloximes (20-23) react with para substituted benzenesulphonyl chlorides ($\underline{A}_1$-$\underline{A}_5$) under identical photochemical conditions at 0°C to give the corresponding sulphones as the exclusive organic products (67-86) in 66-90% yield. No other side product is formed. Chlorocobaloxime is the only inorganic product isolated in each case. The characteristics of all the organic products are given in scheme 2.4, and table 2.5.

Furthermore the following observations are made from the independent experiments:

1. The reaction of (20) with 4-bromobenzenesulphonyl chloride ($\underline{A}_5$) under thermal conditions (refluxing dichloromethane) takes about 12 hr. However, there is no change in yield or nature of product as compared to the corresponding photochemical reaction. However, the same reaction at 0°C without irradiation does not proceed at all and the starting cobaloxime is recovered after 20 hr.

Scheme 2.4




(20) R=2-Thienyl-methyl
- ($\underline{A}_1$) R'=H
- ($\underline{A}_2$) R'=Me
- ($\underline{A}_3$) R'=OMe
- ($\underline{A}_4$) R'=Cl
- ($\underline{A}_5$) R'=Br

(21) R=Furfuryl

(22) R=3-Thienyl-methyl

(23) R=3-Furyl-methyl

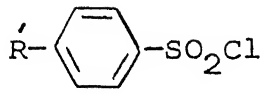
(67) R=2-Thienylmethyl; R'=H
(68) R= '' ; R'=Me
(69) R= '' ; R'=OMe
(70) R= '' ; R'=Cl
(71) R= '' ; R'=Br

(72) R=Furfuryl ; R'=H
(73) R= '' ; R'=Me
(74) R= '' ; R'=OMe
(75) R= '' ; R'=Cl
(76) R= '' ; R'=Br

(77) R=3-Thienylmethyl; R'=H
(78) R= '' ; R'=Me
(79) R= '' ; R'=OMe
(80) R= '' ; R'=Cl
(81) R= '' ; R'=Br

(82) R=3-Furylmethyl ; R'=H
(83) R= '' ; R'=Me
(84) R= '' ; R'=OMe
(85) R= '' ; R'=Cl
(86) R= '' ; R'=Br

Table 2.2: Organic products from the reaction of benzyl cobaloximes (12-17) with benzene sulphonyl chlorides ($A_2$-$A_6$)

| Cobaloxime |  | Organic products ratio* |
|---|---|---|
| (12) | ($A_2$) | (25) 30%; (55) 58%; (61) 8% |
| | ($A_3$) | (26) 40%; (55) 43% |
| | ($A_4$) | (27) 31%; (55) 59% |
| | ($A_5$) | (28) 30%; (55) 55%; (61) 5% |
| | ($A_6$) | (29) 55%; (55) 35% |
| (13) | ($A_2$) | (30) 46%; (56) 21%; (62) 24% |
| | ($A_3$) | (31) 45%; (56) 15% |
| | ($A_4$) | (32) 37%; (56) 43%; (62) 8% |
| | ($A_5$) | (33) 33%; (56) 32%; (62) 20% |
| | ($A_6$) | (34) 67%; (56) 25% |
| (14) | ($A_2$) | (35) 36%; (57) 57% |
| | ($A_3$) | (36) 45%; (57) 22% |
| | ($A_4$) | (37) 30%; (57) 55%; (63) 5% |
| | ($A_5$) | (38) 32%; (57) 23%; (63) 16% |
| | ($A_6$) | (39) 61%; (57) 21%; (63) 8% |
| (15) | ($A_2$) | (40) 39%; (58) 48% |
| | ($A_3$) | (41) 47%; (58) 29% |
| | ($A_4$) | (42) 33%; (58) 49%; (64) 8% |
| | ($A_5$) | (43) 39%; (58) 27%; (64) 18% |
| | ($A_6$) | (44) 64%; (58) 26%; (64) 5% |

...contd.

Table 2.2(contd.)

| | | |
|---|---|---|
| (16) | ($A_2$) | (45) 41%; (59) 9% ; (65) 9% |
| | ($A_3$) | (46) 40%; (59) 5% ; (65) 5% |
| | ($A_4$) | (47) 15%; (59) 35%; (65) 15% |
| | ($A_5$) | (48) 27%; (59) 31%; (65) 17% |
| | ($A_6$) | (49) 59%; (59) 22%; (65) 8% |
| (17) | ($A_2$) | (50) 20%; (60) 17%; (66) 8% |
| | ($A_3$) | (51) 32%; (60) 20%; (66) 5% |
| | ($A_4$) | (52) 8% ; (60) 38%; (66) 6% |
| | ($A_5$) | (53) 15%; (60) 28%; (66) 9% |
| | ($A_6$) | (54) 45%; (60) 30%; (66) 5% |

---

* refers to isolated yields after chromatographic separation.

Table 2.3: Characteristics of Benzyl sulphones (25-54)

| Product No. | M.P. ($^oC$) | $^1H$ NMR Chemical Shift $\delta$ (PPM) (J in $H_2$)† | | | Mass m/e* (Relative abundance) | $\lambda_{max}$/nm ($CH_3OH$) |
|---|---|---|---|---|---|---|
| | | Aromatic | $CH_2$ | Others | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| (25) | 135 | 7.0-7.70(m) | 4.29(s) | 2.39 (Me) | 247(15%),183(47%),182(75%); 91(100%) (A) | 224 |
| (26) | 83 | 6.86(d),7.45(d);6.92-7.30(m) [9] | 4.16(s) | 3.72 (OMe) | 262(66%),199(50%),198(99%), 91(100%) (A) | 240 |
| (27) | 118 | 7.0-7.80(m) | 4.31(s) | - | 268(0.5%),266(0.6%),181(2%), 91(100%) (B) | 229 |
| (28) | 152 | 7.0-7.70(m) | 4.33(s) | - | 312(0.1%),310(3%),181(11%), 91(100%) (B) | 233 |
| (29) | 115 | 7.73(s),7.56(s);7.02-7.33(m) | 4.49(s) | - | 334(4%),181(20%),91(100%) (B) | 236,21 |
| (30) | 150 | 7.72(d),7.43(d),7.29(s) [9] | 4.39(s) | 2.58,2.70 (Me) (Me) | 260(2%),195(0.3%),105(100%) (A) | 222 |
| (31) | 98 | 6.87(d),7.55(d);6.02-7.15(m) [8] | 4.22(s) | 2.30,3.82 (OMe) (Me) | 276(19%),212(18%),105(100%) (A) | 241,22 |
| (32) | 131 | 6.79-7.22(m);7.30-7.70(m) | 4.24(s) | 2.30 (Me) | 282(0.1%),280(0.1%),215(0.1%), 105(100%) (A) | 226 |

...contd.

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| (33) | 152 | 6.97-7.30(m);7.40-7.75(m) | 4.23(s) | 2.33 (Me) | 326(0.2%),324(0.4%),209(11%), 105(100%) (B) | 231 |
| (34) | 184 | 7.55(s),7.72(s);6.91-7.06(m) | 4.42(s) | 2.21 (Me) | (C) | 213,235 |
| (35) | 165 | 7.03(d);7.23-7.58(m) [9] | 4.22(s) | 2.42 (Me) | (C) | 231 |
| (36) | 144 | 6.86(d),7.50(d),7.20-7.40(m) [8] | 4.09(s) | 3.86 (OMe) | (C) | 237 |
| (37) | 155 | 7.02(d);7.25-7.65(m) [8] | 4.24(s) | - | (C) | 226 |
| (38) | 136 | 7.03(d);7.30-7.90(m) [9] | 4.28(s) | - | (C) | 231 |
| (39) | 199 | 7.26(s),7.52(s) 6.75(d),7.06(d) [9] | 4.12(s) | - | (C) | 226,212 |
| (40) | 152 | 7.03(d),7.56(d);7.20-7.44(m) [9] | 4.23(s) | 2.39 (Me) | 280(5%),279(14%),216(1%), 215(0.4%),125(100%) (A) | 225 |
| (41) | 151 | 6.90(d),7.48(d);7.30(d),7.05(d) [8] [9] | 4.16(s) | 3.86 (OMe) | 298(5%),296(14%),232(22%), 125(100%) (A) | 226,239 |
| (42) | 143 | 7.03(d),7.85(d);7.45-7.70(m) [9] | 4.26(s) | - | (C) | 226 |
| (43) | 148 | 7.10(d),7.40(d);7.52-7.80(m) [9] | 4.26(s) | - | (C) | 231 |

...contd.

| 1 | 2 | 3 | 4 | 5 | 6 | |
|---|---|---|---|---|---|---|
| (44) | 205 | 7.92(s),7.69(s);7.10-7.40(m) | 4.59(s) | - | (C) | 21( |
| (45) | 198 | 7.12-7.36(m);7.45-7.67(m) | 4.30(s) | 2.39 (Me) | 271(28%),207(8%),116(100%) (A) | |
| (46) | 112 | 6.92(d),7.21(d);7.42-7.82(m) [9] | 4.30(s) | 3.78 (OMe) | 287(4%),223(0.8%),116(100%) (A) | |
| (47) | 159 | 7.28(d),7.65(d);7.40-7.60(m) | 4.37(s) | - | 293(1%),291(3%),231(3%),116(100%) (B) | |
| (48) | 138 | 7.27(d);7.45-7.78(m) [9] | 4.35(s) | - | 337(1%),335(1%),231(5%),116(100%) (B) | |
| (49) | 140 | 7.96(s),7.75(s);7.20-7.65(m) | 4.63(s) | - | 361(1%),359(1%),231(4%),116(100%) (B) | |
| (50) | 157 | 7.22(d);7.40-7.80(m) [9] | 4.33(s) | - | (C) | 22 |
| (51)** | | 7.0-8.2(m) | 4.70(s) | 4.10 (OMe) | - | - |
| (52) | | 7.0-8.1(m) | 4.55(s) | - | - | - |
| (53) | | 7.1-8.2(m) | 4.50(s) | - | - | - |
| (54) | | 7.2-8.1(m) | 4.65(s) | - | - | - |

† All spectra are run on EM 390(90 MHz) spectrophotometer.

* (A) refers to $M^+$, $M-SO_2$, R or $M^+$, $M-SO_2$, $M-SO_2-H$,R.

(B) refers to $M^+$,(R-R)-H,R.

(C) refers to no clear pattern.

** Compounds (51-54) are slightly impure.

I.R. absorptions for all compounds lie within 1160-1180 $cm^{-1}$ ($\nu_{sym}$) and 1275-1350 $cm^{-1}$ ($\nu_{asym}$)

Table 2.4: Characteristics of bibenzyls (55-60)

| Compound No. | Compound | M.P. (°C) | $^1$H NMR Chemical shift: δ(ppm) | |
|---|---|---|---|---|
| | | | Aromatic | $CH_2$ |
| (55) | $C_6H_5CH_2CH_2C_6H_5$ | 51 | 7.1-7.4(m) | 2.9(s) |
| (56) | 4-$MeC_6H_4CH_2CH_2C_6H_4$-Me-4 | 75 | 7.08(s) | 2.86* (s) |
| (57) | 4-$BrC_6H_4CH_2CH_2C_6H_4$-Br-4 | 113 | 6.98,7.36[a] (9 Hz) | 2.84(s) |
| (58) | 4-$ClC_6H_4CH_2CH_2C_6H_4$-Cl-4 | 98 | 7.02,7.24[a] (9 Hz) | 2.86(s) |
| (59) | 4-$CNC_6H_4CH_2CH_2C_6H_4$-CN-4 | 198 | 7.16-7.94(m) | 3.36(s) |
| (60) | 4-$NO_2C_6H_4CH_2CH_2C_6H_4$-$NO_2$-4 | 180 | 7.23,8.1[a] (9 Hz) | 3.08(s) |

*($CH_3$ δ2.3); a: $A_2B_2$ pattern is clearly observed and coupling constant is given in parentheses.

Table 2.5: Characteristics of heteroaromatic methyl sulphones, (67-86)

| Product No. | M.P. (Yield%) | $^1$H NMR Chemical Shifts δ (PPM) [J in Hz] | | | | Mass$^{++}$ m/e (Relative abundance) | $\lambda_{max}$/nm ($CH_3OH$) |
|---|---|---|---|---|---|---|---|
| | | Heteroaromatic | Aromatic | $-CH_2$ | Other | | |
| 1 | | 2 | 3 | 4 | 5 | 6 | 7 |
| (67) | 82 (60) | 7.20(m),6.84(m),6.76(d) [4] | 7.42(m),7.54(m),7.64(m) | 4.46(s) | - | 238(8%),173(10%),97(100%) (A) | 237,217 |
| (68) | 125 (61) | 7.23(m),6.85(m),6.76(d) [4] | 7.55(d),7.23**(m) [4] | 4.49(s) | 2.39 (Me) | 252(5%),187(5%),97(100%) (A) | 226 |
| (69) | 120 (69) | 7.23(m),6.70-6.85**(m) | 7.56(d),6.85**(m) [9] | 4.42(s) | 3.62 (OMe) | 268(4%),203(2%),97(100%) (A) | 225 |
| (70) | 94 (73) | 7.21(m),6.76-6.85(m) | 7.55(d),7.37(d) [7] | 4.43(s) | - | 272(0.2%),193(4%),97(100%) (B) | 229 |
| (71) | 105 (75) | 7.28(m),6.84(m),6.78(m) | 7.46(d),7.54(d) [7] | 4.46(s) | - | 318,(1%),193(15%),97(100%) 316 (1) (B) | 233 |
| (72) | 58 (80) | 6.27(d),7.30(s) [5] | 7.45-7.81(m) | 4.39(s) | - | 222(10%),157(3%),81(100%) (A) | 220 |
| (73) | 100 (65) | 6.28(d),7.30(s) [5] | 7.51(d),7.30(d)** | 4.35(s) | 2.39 (Me) | 236(8%),171(4%),81(100%) (A) | 223 |

...contd.

Table 2.5(contd.)

| 1 | | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| (74) | 81 (70) | 6.29(d),7.33(s) [5] | 6.97(d),7.64(d) [9] | 4.39(s) | 3.89 (OMe) | 252(5%),187(1%),81(100%) (A) | 241 |
| (75) | 113 (73) | 6.33(d),7.32(s) [5] | 7.51(d),7.71(d) [9] | 4.40(s) | - | 256,(2%), 161(50%),81(100%) 258 (1%) (B) | 226 |
| (76) | 127 (63) | 6.30(d),7.31(s) [5] | 7.52(d),7.60(d) [3.3] | 4.38(s) | - | 300,(2.5%),161(3%),81(100%) 302(2.5 %) (B) | 233 |
| (77) | 115 (60) | 6.92(m),7.04(d),7.24(m) [2] | 7.46-7.83(m) | 4.39(s) | - | 238(5%),173(3%),97(100%) (A) | 216,232 |
| (78) | 88 (62) | 6.92(m),7.03(d),7.21(m) [2] | 7.21**(m),7.52(d) [6] | 4.33(s) | 2.43 (Me) | 252(10%),187(5%),97(100%) (A) | 224 |
| (79) | 79 (67) | 6.92(m),7.04(d),7.26(m) [2] | 6.92**(m),7.50(d) [8] | 4.34(s) | 3.84 (OMe) | 268(0.5%),203(5%),97(100%) (A) | 239 |
| (80) | 107 (69) | 6.92(m),7.06(d),7.28(m) [2] | 7.42(d),7.58(d) [8] | 4.38(s) | - | 272(7%),193(2%),97(100%) 274(3%) (B) | 226 |
| (81) | 118 (74) | 6.90(m),7.04(d),7.26(m) [2] | 7.52(d),7.64(d) [4] | 4.39(s) | - | 316(10%),193(98%),97(100%) 318(11%) (B) | 234 |
| (82) | 88 (81) | 6.26(s),7.23(s),7.36(s) | 7.40-7.90(m) | 4.19(s) | - | 222(2%), 158(15%),81(100%) (A) | 216 |
| (83 | 103 (90) | 6.33(s),7.22(s),7.38(s) | 7.30(d),7.62(d) [7] | 4.16(s) | 2.43 (Me) | 236(2%), 172(7%) ,81(100%) (A) | 222 |
| (84) | 77 (72) | 6.25(s),7.23(s),7.33(s) | 6.93(d),7.67(d) [9] | 4.16(s) | 3.89 (OMe) | 252(1%), 188(29%),81(100%) (A) | 240 |

...contd.

Table 2.5(contd.)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| (85) | 87<br>(87) | 6.28(s),7.23(s),7.34(s) | 7.48(d),7.68(d)<br>[7] | 4.23(s) | - | 256(8%),<br>258(2.5%) | 192(14%),81(100%)<br>194(4%)<br>(A) | 224 |
| (86) | 102<br>(79) | 6.27(s),7.21(s),7.33(s) | 7.65(s) | 4.19(s) | - | 300(4%),<br>302(5%) | 236(12%),81(100%)<br>238(11%)<br>(A) | 234 |

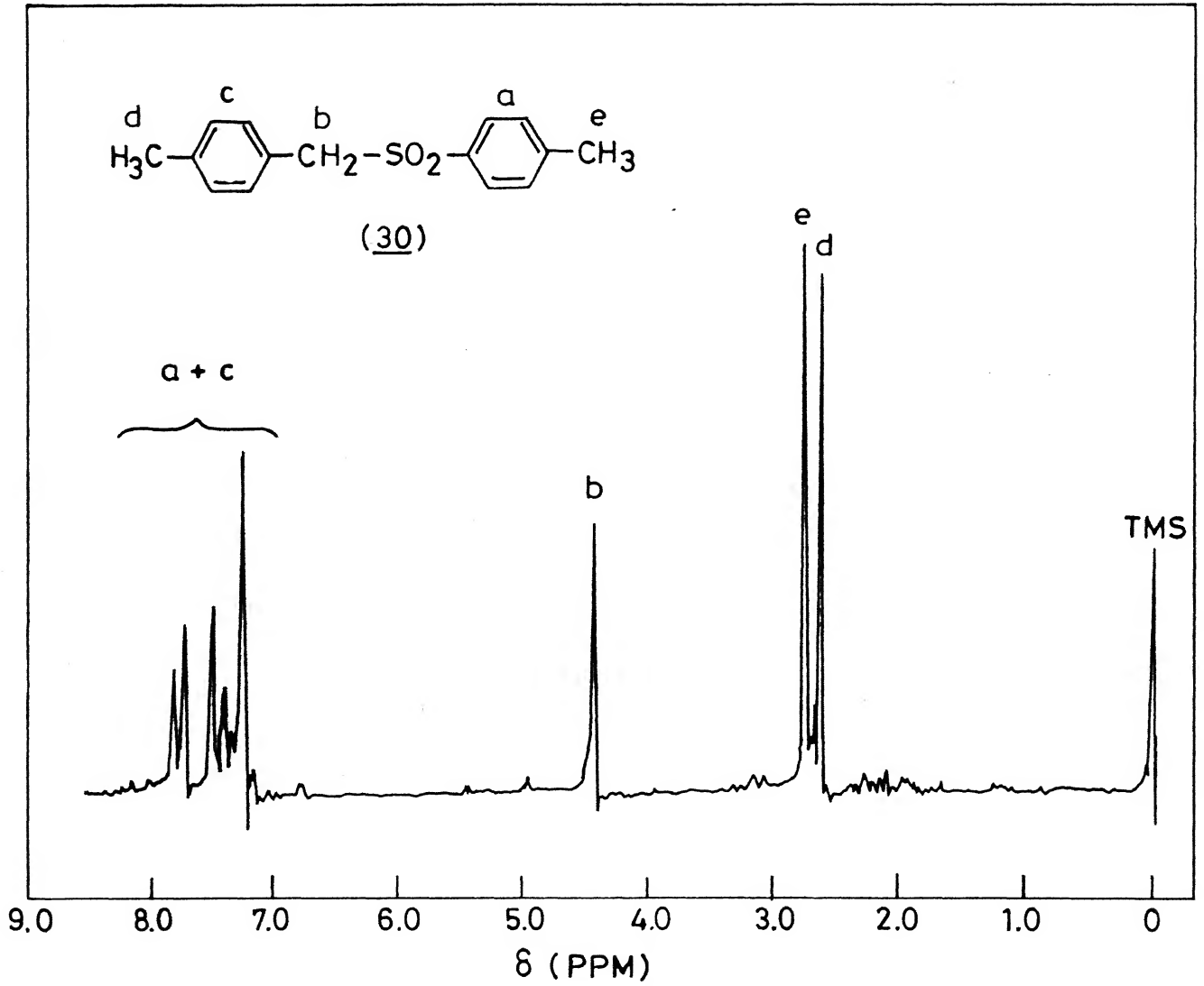
* 400 MHz spectra (The rest are taken on 90 MHz machine)

** Partly obscured

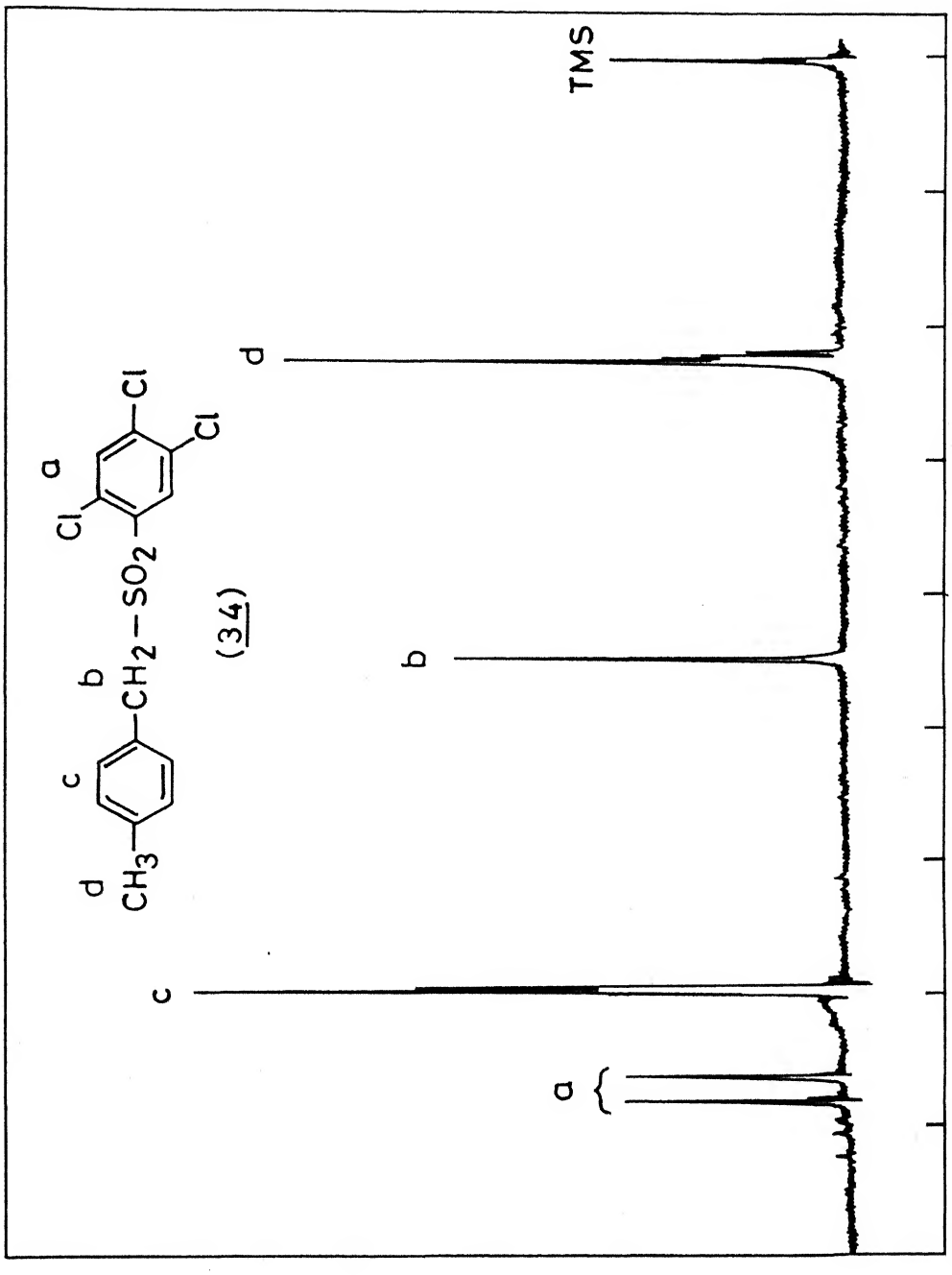
For (77) to (81), the doublet is well resolved only in 400 MHz spectrum

†† A = $M^+$, M-$SO_2$-H, R

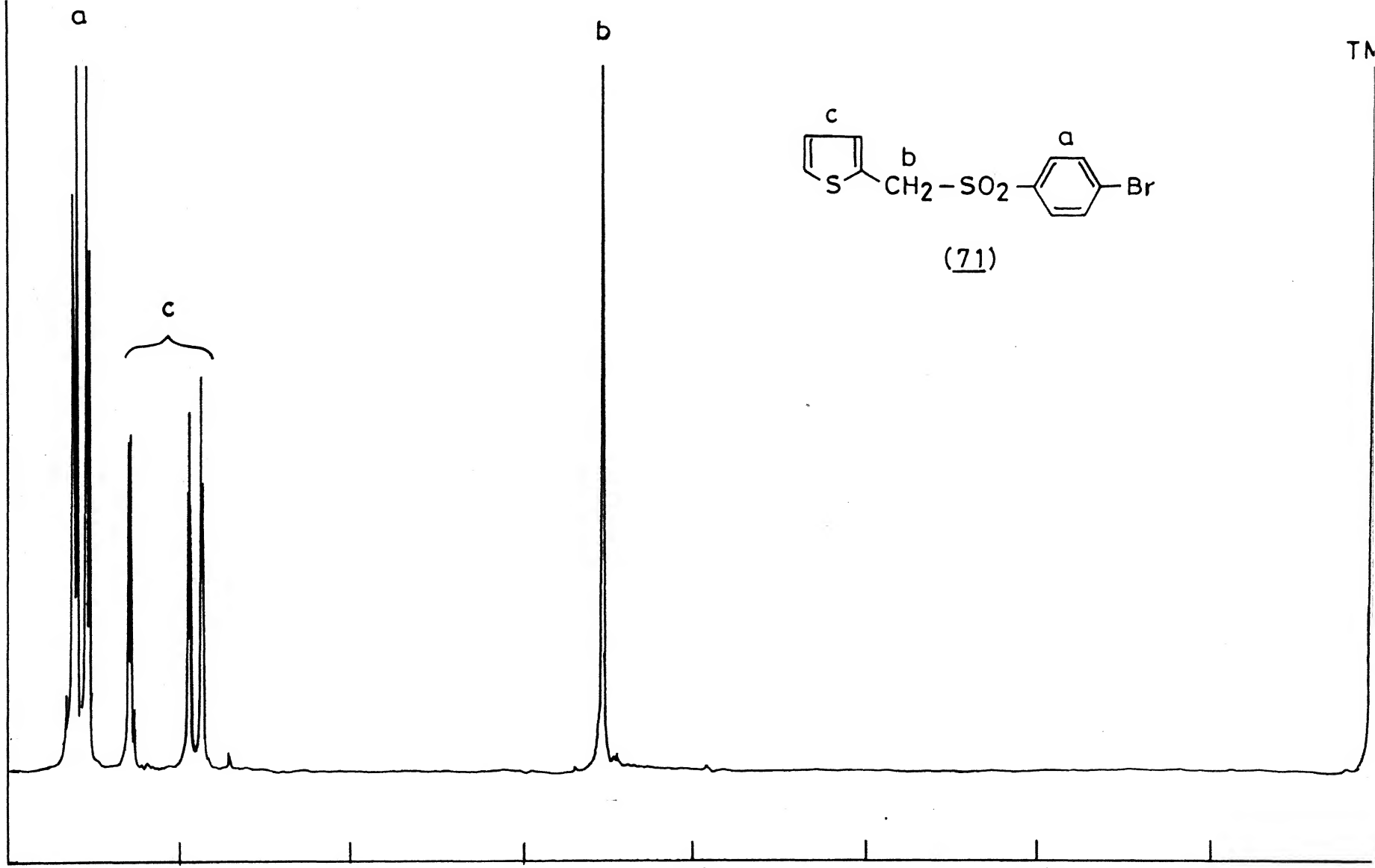
B = $M^+$, R-R-H, R .



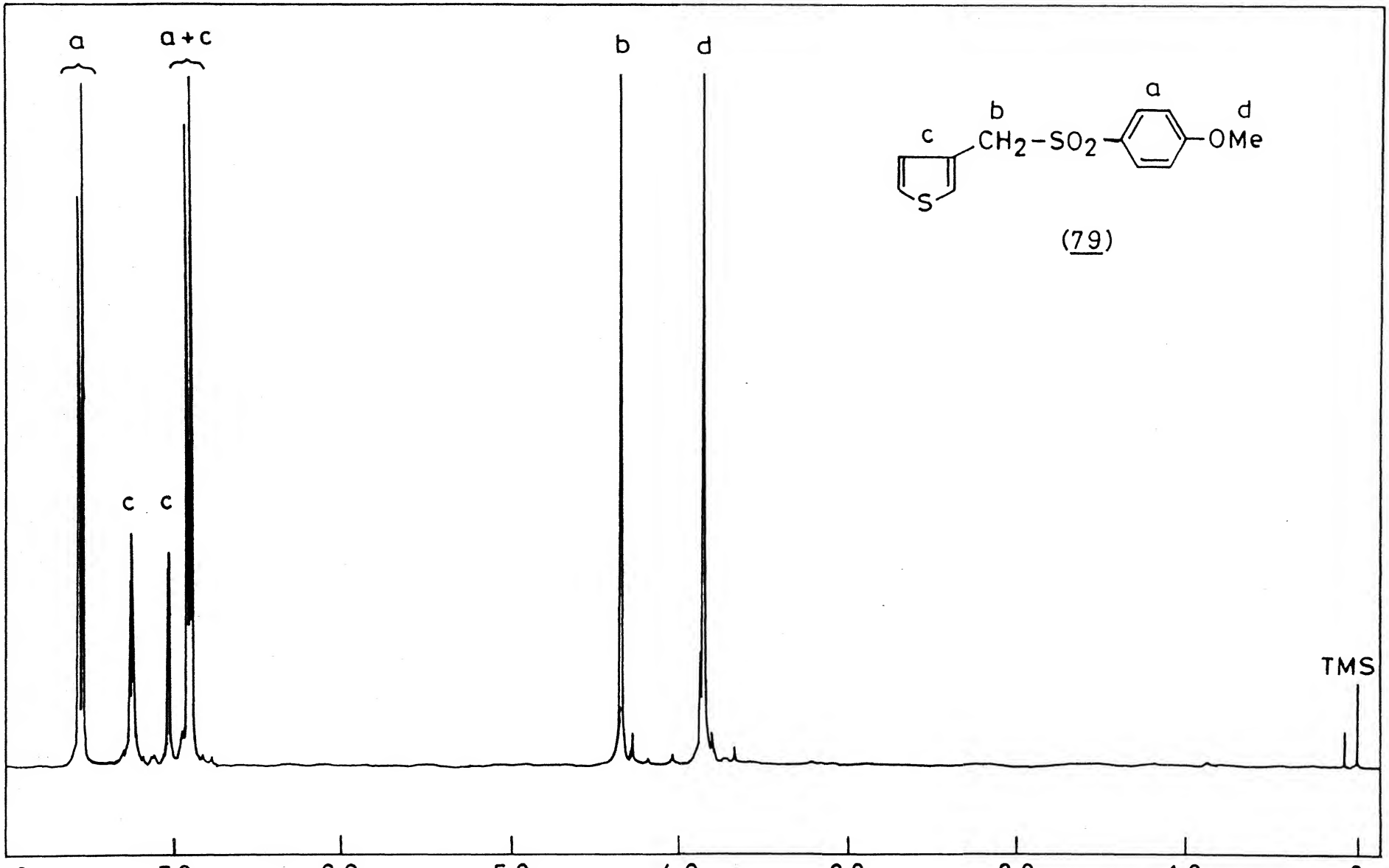

$^1H$ NMR Spectrum (90 MHz) of (30)




$^1$H NMR Spectrum (90 MHz) of (34)

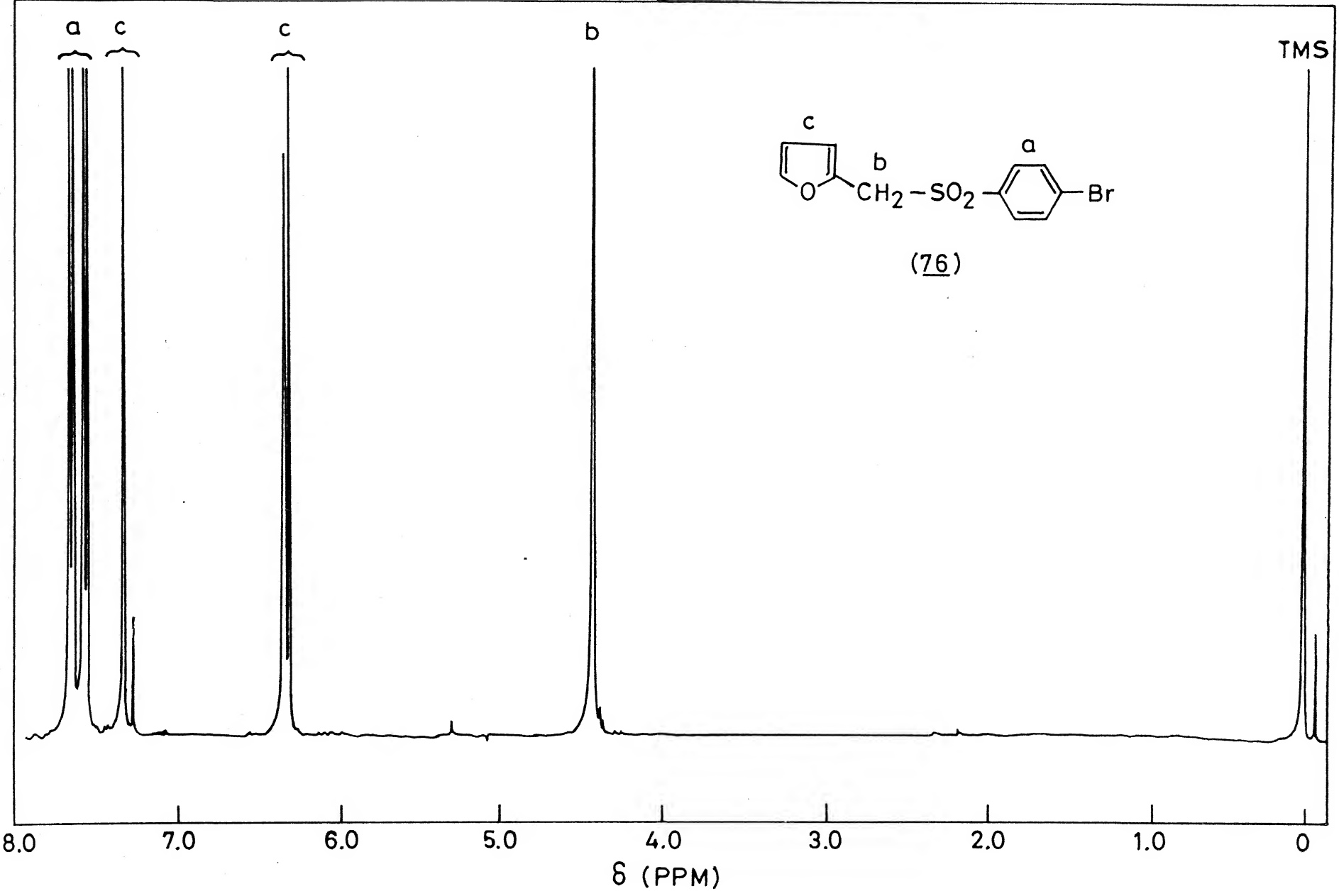



$^1$H NMR Spectrum (400 MHz) of (71)



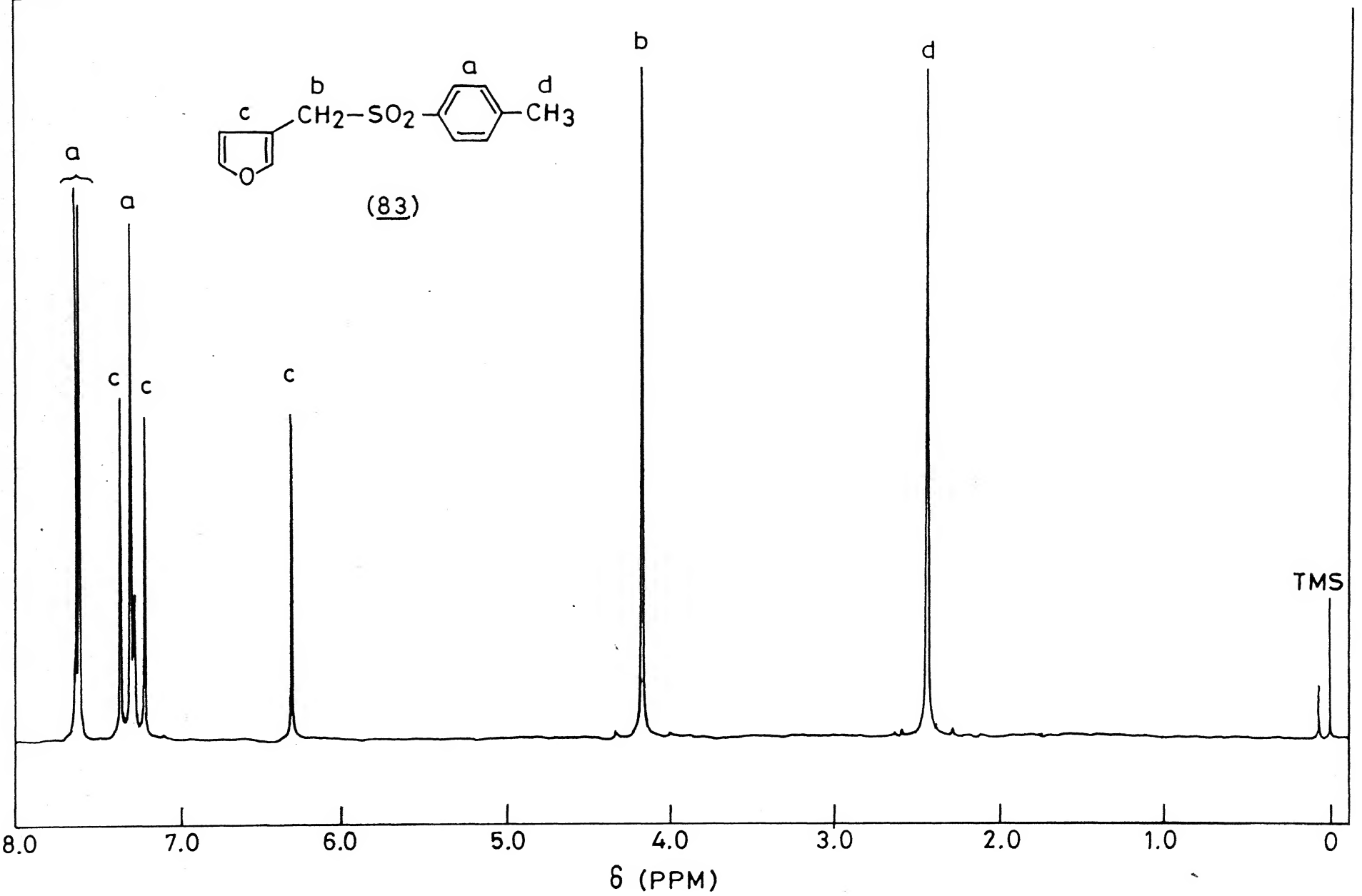

(79)

$^1$H NMR Spectrum (400 MHz) of (79)




(76)

$^1$H NMR Spectrum (400 MHz) of (76)




$^1$H NMR Spectrum (400 MHz) of (83)

2. The reaction of organocobaloximes with aged samples of arylsulphonyl chloride having the corresponding sulphonic acid impurity affords sulphones in lower yields. The decrease in yield depends upon the amount of sulphonic acid present.

3. The reaction of benzylcobaloxime (12) with 4-methyl benzene sulphonyl chloride ($\underline{A}_2$) in Srinivasan's photoreactor (irradiation by 400 W medium pressure mercury lamp) at 25°C takes only 1 hr. However, the yield of the sulphone is much less as compared to the corresponding reaction under photochemical conditions at 0°C. The products formed are (25) 9% , (55) 62% , (61) 12% (scheme 2.3).

4. The change of equatorial ligand in organocobaloximes does not affect the nature and yield of the reaction product, for example,the reaction of 2-thienylmethyl bis(cyclohexane-glyoxime)pyridine cobalt(III) with 4-methylbenzene sulphonyl chloride ($\underline{A}_2$) under photochemical conditions forms sulphone (67) in identical yield to that of the reaction of (20) with ($\underline{A}_2$).

5. 2-Benzofuryl methyl cobaloxime reacts rather slowly (~6 hr) with 4-methylbenzene sulphonyl chloride ($\underline{A}_2$) under photochemical conditions to form the corresponding sulphone, 2-benzofuryl methyl-4-tolylsulphone in 60% yield, m.p. 178°C, 400 MHz $^1$H NMR: ($CDCl_3$), δ, 7.72-7.71 (m, aromatic, 8H),

6.68 (s, 1H), 4.56 (s, $-CH_2$), 2.44 (s, $CH_3$). Mass m/e: 286 (6%), 221 (3%), 131 (100%), U.V. $\lambda_{max}$/nm ($CH_3OH$): 278, 270, 250.

2.3.3 Discussion

All the reactions described in this chapter are free radical in nature. Although the evidence is indirect, it is certain that the free radicals abound under all the conditions described. Since, the cleavage of the Co–C bond is a key feature of the reactions of these substances, it is important to examine the tendency of the organocobaloximes to undergo unimolecular homolysis. It is well established that homolysis of the Co–C bond in organocobaloximes take place very readily even on irradiation at wavelengths greater than 360 nm.[166,275] This is consistent with the low Co–C bond energy 17–25 kcal $mol^{-1}$ in such substrates.[109,110,249,276] The low value of the Co–C bond energy and its high valent nature suggest that it is much weaker compared to other metal–carbon bonds and is susceptible to homolytic cleavage which may even be effected by visible radiation. Tungsten lamps and glass apparatus are therefore, adequate for preparative photolysis experiments. Cobaloxime(II), a $d^7$ species, formed on the homolysis of the Co–C bond has been shown to be a good leaving group in many such similar reactions.[150a,174,262] Unlike the conventional organic free radicals, it can be easily prepared and can be stored in inert atmosphere indefinitely in certain solvents. It neither disproportionates nor dimerses in neutral solvents. Organosulphonyl chlorides, $RSO_2Cl$, have been identified previously as chain propagating species in many organic

reactions of alkenes and its potential as free radical precursors is well established in literature.[277]

The nature of the products and the influence of initiators/inhibitors on the rates of reaction point to the free radical nature of these reactions and we believe that a chain reaction is involved in which organosulphonyl radical $\dot{R}SO_2$ and cobaloxime (II) are the chain carrying species (Scheme 2.5). These reactions are subject to concentration dependent induction periods, especially where the materials are fresh and pure. However, the formation of a mixture of products like sulphones, bibenzyls and benzyl ethers of dimethylglyoxime indicates that the reaction of benzylcobaloximes with organosulphonyl chlorides under thermal and photochemical conditions certainly proceeds by a mixture of mechanisms. The formation of substantial amounts of bibenzyls in each reaction is indicative of the presence as intermediates of benzyl radicals, which are known to dimerise fast (eqn. 5). The sulphone, however may arise by a homolytic substitution of $\dot{R}SO_2$ at the α carbon of the organocobaloxim (eqn. 3) generating cobaloxime(II) which forms part of a chain reaction by abstracting chlorine atom from $RSO_2Cl$ to give another propagating species $\dot{R}SO_2$ (eqn. 2).

A trace amount of cobaloxime(II) present in all organocobaloximes is sufficient enough to initiate the reaction. The initiation can also be achieved by thermolysis or photolysis of benzylcobaloximes (eq. 1). The organosulphonyl radical $R'\dot{S}O_2$, generated by abstraction of halogen atom from the sulphonyl chloride by cobaloxime(II) attacks the α carbon atom of the benzylcobaloxime, displacing the cobaloxime(II) and forms the product.

Scheme 2.5

Initiation

$$RCH_2Co^{III}(dmgH)_2Py \rightleftharpoons R\dot{C}H_2 + Co^{II}(dmgH)_2Py \quad \ldots (1)$$

Propagation

$$Co^{II}(dmgH)_2Py + R'SO_2Cl \rightleftharpoons ClCo^{III}(dmgH)_2Py + R'\dot{S}O_2 \quad \ldots (2)$$

$$R'\dot{S}O_2 + RCH_2Co^{III}(dmgH)_2Py \longrightarrow RCH_2SO_2R' + Co^{II}(dmgH)_2Py \quad \ldots (3)$$

Termination

$$R'\dot{S}O_2 + R\dot{C}H_2 \longrightarrow R'SO_2CH_2R \quad \ldots (4)$$

$$R\dot{C}H_2 + R\dot{C}H_2 \longrightarrow RCH_2CH_2R \quad \ldots (5)$$

$$R'\dot{S}O_2 + Co^{II}(dmgH)_2Py \longrightarrow R'SO_2Co^{III}(dmgH)_2Py \quad \ldots (6)$$

The proof for $R'\dot{S}O_2$ and cobaloxime(II) as propagating species comes from the earlier observation that the $^1H$ NMR spectrum of allylcobaloxime in $CDCl_3$ shows a dynamic equilibrium as a result of cobalt-for-cobalt displacement reaction and secondly addition of trace amount of tosyl chloride to the solution causes a marked decrease in the extent of dynamic character, and the latter again becomes evident in the $^1H$ NMR spectrum when the added sulphonyl chloride has been consumed.[92,278] Furthermore, the reaction of cobaloxime(II) with tosyl chloride gives good

yield of chlorocobaloxime and organosulphonylcobaloxime $4\text{-}CH_3C_6H_4SO_2(Co^{III})$.[278] This result further supports the plausibility of the proposed termination step in scheme 2.5. Though $S_H2$ process is the main process responsible for the formation of sulphones in these reactions, we cannot rule out some ancilliary process in which the formation of the latter may arise by the combination of benzyl radicals and sulphonyl radicals (eq. 4). The formation of $R'SO_2Co^{III}(dmgH)_2Py$ supports this view point (eq. 6). However, it is very difficult to estimate the proportion of reaction through these two processes. In view of the fact that the observed reactions are chain reactions and the rate of propagation step must be more than the termination step in these reactions, the formation of benzylsulphones totally by the combination process is ruled out.

Benzyl ethers of dimethylglyoxime is formed as side products in certain reactions only and such a product is completly absent in reactions done in presence of excess of pyridine, when six coordinate organocobaloxime is the predominant species present in solution. This suggests that ether formation must be an artefact of oxidation process on the intermediate five coordinate organocobaloxime complex.

Though a six coordinate octahedral configuration is the most abundant for Co(III) complexes and a penta coordinate base free complex is found less frequently as a stable form, the

latter is however postulated as an intermediate in many ligand exchange reactions.[101,152a,206,329] The importance of five co-ordinate complex is also noted for iron complexes where molecular oxygen reacts easily with five co-ordinate iron(II) porphyrin complex to give $\mu$-oxo iron(III) dimers.[279] The six coordinate base on form is unreactive, however. Thus, base free five coordinate complexes are expected to contribute as reactive intermediates in reactions of cobalt complexes other than ligand exchange processes such as oxidation reductions, but little is known so far. The contribution of a five coordinate base free form in the reaction of molecular oxygen with alkyl cobaloximes is reported[280] but the results are criticised later.[188a] Recently the iodination of para substituted benzyl-cobaloximes is shown to occur via a base free five coordinate species.[281] We have recently observed that the reaction of benzyl and substituted benzyl cobaloximes with thiocyanogen proceeds via a base free pentacoordinate organocobaloxime as intermediate species.[183] An additional support for such base free five coordinate cobalt(III) complexes in the present study comes from the recently reported kinetic data on the dissociation of pyridine in the benzyl and para substituted benzylcobaloximes.[281] The high rates indicate that dissociation of pyridine is a very facile process in such complexes. Therefore, the attack of $\dot{R}SO_2$ on the cobalt, effectively a reversible one electron oxidation process, is not unlikely in the present studies.

In the earlier work on benzylcobaloximes with polyhalogenomethyl radicals,[173b,282] the formation of such side products has been ascribed to the unimolecular homolysis of Co–C bond at higher temperature (~60°C) and the benzyl radical so formed either dimerises or abstracts a halogen atom from the polyhalogenomethyl halide. As the reactions in the present study are carried out under very mild conditions, the unimolecular homolysis of benzyl cobaloxime (eq. 1) may be neglected except in so far as it provides a means of initiation of the chain. The bulk of bibenzyl may thus be a result of the induced homolysis of the Co–C bond caused by the attack of the sulphonyl radical at a site other than the α carbon of the benzyl ligand i.e. at a peripheral hydrogen, at a C=N bond of the equatorial ligand, at the metal (scheme 2.6) or possibly by an outer sphere electron transfer.

$$Ar\dot{S}O_2 + RCH_2Co^{III}(dmgH)_2Py \longrightarrow ArSO_2Co^{III}(dmgH)_2Py + R\dot{C}H_2 \quad \ldots (7)$$

However, the contribution from the process of (eq. 7) is negligible since such an attack does not occur on the six coordinate benzyl cobaloximes as indicated by our results. As the concentration of $RCH_2$ radicals in solution at a given time is almost a trace the alternative process of (eq. 8) is not taken into account.

$$R\dot{C}H_2 + ArSO_2Cl \longrightarrow RCH_2SO_2Ar + \dot{C}l \qquad \ldots (8)$$

The bulk amount of bibenzyl formed by the dimerisation of benzyl radicals, must arise by the following scheme 2.6.

Scheme 2.6

$$RCH_2Co^{III}(dmgH)_2Py \underset{+Py}{\overset{-Py}{\rightleftharpoons}} RCH_2Co^{III}(dmgH)_2 \overset{Ar\dot{S}O_2}{\rightleftharpoons} RCH_2Co^{IV}(dmgH)_2SO_2Ar$$

$$RCH_2Co^{IV}(dmgH)_2SO_2Ar \longrightarrow ArSO_2Co^{III}(dmgH)_2Py \underset{-Py}{\overset{+Py}{\rightleftharpoons}} R\dot{C}H_2 + Co^{III}(dmgH)_2SO_2Ar$$

The formation of $ArSO_2Co^{III}(dmgH)_2Py$ and benzyl ether of dimethylglyoxime justifies scheme 2.6 and is further indicative of the intermediate formation of organocobalt(IV) species in solution since dimethylglyoxime ether is a characteristic decomposition product of organocobalt(IV) species in solution. Similar ether products have been observed as side products in many reactions of organocobaloximes with electrophilic free radical precursors.[210,211,261,282]

The significant increase in the yield of the sulphones when pyridine is present in excess is ascribed to the fact that the six coordinate complex is the reactive species which may

i) enhance the rate of reaction of (eq. 3) (Scheme 2.5).

ii) prevent the alternative pathway (Scheme 2.6) partially or completly in which the free radical $Ar\dot{S}O_2$ attacks the five coordinate metal and leads to the formation of benzyl radicals.

The formation of sulphones as the exclusive organic product in high yield in the reactions of heteroaromatic methyl cobaloximes (20-23) with organosulphonyl chlorides supports the above view point. The reaction in these cases is much cleaner probably because of the following reasons.

a) In our recent work on the halogenation of heteroaromatic methylcobaloximes it is observed that the Co-C bond is much more nucleophilic as compared to the corresponding Co-C bond in benzylcobaloximes,[203] hence the attack of electrophilic free radical $Ar\dot{S}O_2$ on the α carbon of organocobaloxime (eq. 3) becomes more facile.

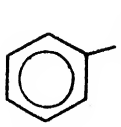
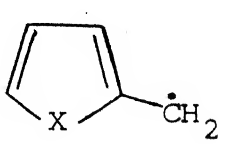
b) The one electron oxidation potential of heteroaromatic methyl cobaloximes are higher as compared to the benzyl cobaloximes,[183] hence the intermediate organocobalt(IV) species responsible for the formation of ether products is not formed. It is to be noted that the corresponding dimethylglyoxime ether products are exclusively formed in the reaction of heteroaromatic methyl cobaloximes and Mn(III) acetate that will be discussed latter.

c) In view of the low trans effect of the heteroaromatic methyl group as compared to the benzyl group, the axial base ligand, pyridine, is not labile and remains intact with the cobalt.[183e] With the result the intermediate five coordinate cobaloxime complex, required for the attack of $R\dot{S}O_2$ on cobalt, is not formed. The formation of dimerisation product is thus prevented.

Finally, the lowering in yields when the reactions are done with aged samples of arylsulphonyl halides having the corresponding sulphonic acid as impurity is attributed to the fact that one of the propagating species, $Co^{II}(dmgH)_2Py$, decomposes almost instantaneously with acids to give $Co^{II}(aq.)$ complex.[283] Thus one of the propagating species is lost.

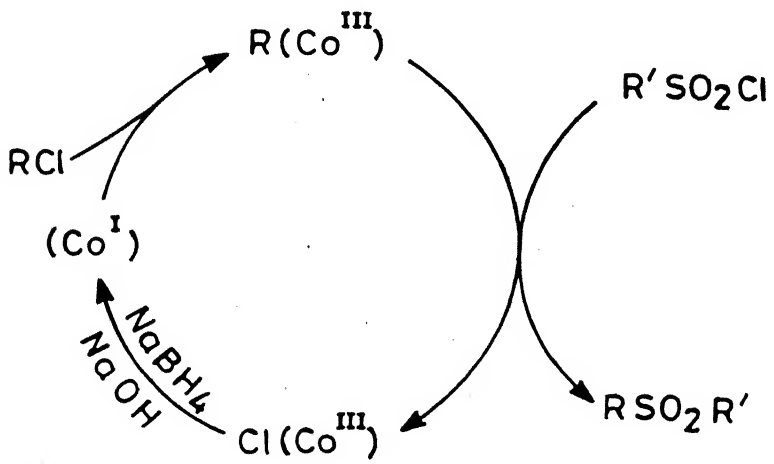
The reactions described in this paper also have some bearing on the recent work on the sulphurdioxide insertion reactions.[173a] It has been proposed that one of the key step might be the attack of the sulphonyl radical $Ar\dot{S}O_2$, formed on capture of an organic radical by $SO_2$, on the metal of the organometallic substrate, thereby regenerating the organic radical $R^{\bullet}$ (eq. 9).

$$Ar\dot{S}O_2 + RCo^{III}(dmgH)_2Py \longrightarrow ArSO_2Co^{III}(dmgH)_2Py + R^{\bullet} \quad .. \quad (9)$$

R =  , 

Our results clearly indicate that such a process does not take place, other than as a minor path, because the organosulphonyl radicals preferentially attack the carbon centre and organosulphonyl cobaloximes are the minor by products of these reactions, formed as a result of the chain termination step (eq. 6) (Scheme 2.5).

The work described in the present study is important in view of the ready formation of a wide range of benzyl and heteroaromatic methyl cobaloximes in high yield from the corresponding halides and bis(dimethylglyoximato)pyridine cobalt(I) ion and their straight forward reaction with organosulphonyl chloride provides the convenient route for the preparation of sulphones by the novel $S_H2$ process.



# CHAPTER - 2B

## REACTIONS OF ORGANOCOBALOXIMES WITH Mn(III)ACETATE

## 2.4.1 Background

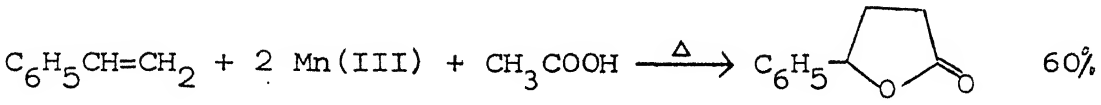
The importance of $S_H2$ reactions at saturated carbon centre has already been highlighted earlier and it is obvious that such reactions have a great synthetic potential in organic chemistry. Besides free radical carbon to carbon bond forming reactions have become part of the day to day armoury of the synthetic chemist.

Highly oxidised transition metals have long been used in organic synthesis (i.e. Cr(VI) in $H_2Cr_2O_7$ and Mn(VII) in $KMnO_4$) and their synthetic and mechanistic chemistry has been thoroughly studied.[284a] Even so new uses are being discovered every year for these standard reagents.[284b] Similarly, high valent state of vanadium, cerium, lead etc. have also been tested successfully for the synthesis of organic moities. However, milder transition metal oxidants like Mn(III) species have been far less commonly employed by synthetic chemists. Mn(III) acetate* which can be very readily synthesised from Mn(II) acetate and potassium permanganate in acetic acid and can be stored for extended period of time, has been shown to be a good source of $\dot{C}H_2COOH$ radicals when heated at 150°C.[285]

---

* X ray structure of anhydrous Mn(III) acetate shows it to be an oxocentered triangle of three manganese atoms held together by six bridging acetate ligands. As such, a single Mn(III) acetate is capable of performing upto three sequential one electron oxidations of a substrate while each Mn(III) is reduced to Mn(II).

It has been shown that Mn(III) acetate in acetic acid at reflux temperature converts a variety of olefins (generally used in excess) to γ-lactones as illustrated by the following example.[285]




Recently it has been shown that the olefinsundergo carbo-lactonization reaction much more readily in the presence of Mn(III) acetate & cyanoacetic acid in acetic acid at 23°C.[286]

Since free radicals of the kind $\dot{C}H_2COOH$ are involved in such reactions and there are few examples of the homolytic displacement reactions at a saturated carbon centre, it seems worthwhile to try to prepare substituted acetic acids, $RCH_2COOH$, by a $S_H2$ reaction between this radical and benzylcobaloximes. One should not over-look the possibility of organocobaloxime getting oxidised. Even if this is so, this will in turn throw some light on the organocobalt(IV species formed in solution and its decomposition process about which a mention has already been made earlier.

## 2.4.2 Experimental

The general experimental procedure including details of solvents, gases, chromatography, physical measurements and instruments are same as those described earlier under section 2.2.

### Starting materials and cobaloximes

Glacial acetic acid, acetic anhydride, sodium acetate, Mn(II) acetate, cyanoacetic acid, were commercial materials and were used as such. Mn(III) acetate dihydrate was prepared by a modified procedure of christenson and is outlined below.[287]

In a 500 ml three necked flask fitted with a stirrer, condenser and thermometer, Mn(II) acetate $4H_2O$ (10.7 g) in glacial acetic acid (150 ml) was heated to 110°C. Ground $KMnO_4$ (17.0 g) was added in small portions through the condenser over a period of 20 minutes while the temperature was maintained at 110°C. The reaction mixture was heated for additional 20 minutes, cooled, poured into water (150 ml) and left overnight. The solid product was filtered out, washed with ether and air dried. Yield (12.4 g, 82%).

Benzyl and substituted benzyl cobaloximes (12-19) and furfuryl cobaloxime (21) were prepared as described on page 91. C-bonded methylene-Y-phenylcobaloximes (Y = O,S, NH), were received as gift from Dr. Manoj Kumar, a fellow worker in our laboratory.

Reaction of Mn(III) acetate.$2H_2O$ with organocobaloximes

The following general method was used for all reactions: In a typical experiment, a solution of 4-cyanobenzylcabaloxime (16) (0.5 g; 1.03 mmol), Mn(III) acetate.$2H_2O$ (0.6 g, 2.2 mmol), sodium acetate (0.5 g, 6.1 mmol) in 15 ml glacial acetic acid and 3 ml acetic anhydride was heated to 150°C. The progress of reaction which took less than 90 minutes to complete was monitored by TLC on silica gel using ethylacetate as eluent. The reaction was worked up by addition of water and then extraction with solvent ether. The product was obtained as white solid (73%) and was further recrystallised from petrolium ether. The same reaction was also carried out with Mn(III) acetate under following modifications.

(i) at temperatures 90°, 60°, 25° instead of 150°C

(ii) when no acetic anhydride was added

(iii) reaction was done under nitrogen atmosphere

(iv) reaction was done in the presence of cyanoacetic acid at 23°C, 40°C, 70-80°C and also at 0°C under irradiation (2 x 200W tungsten lamps)

The reaction was also carried out at 150°C without the presence of Mn(III) acetate with benzylcobaloxime (12). A white crystalline product was obtained m.p. 98°C, [NMR $CDCl_3$ $\delta$ 2.29] which could not be characterised.

## 2.4.3 Results

All the reactions are carried out in glacial acetic acid at 150°C. A single organic product is obtained in each case (scheme 2.7) and are identified by $^{1}H$ NMR as benzyl ethers of dimethylglyoxime (61-66), (87-90). The same reactions done in different conditions mentioned above (i-iv), do not lead to a change of product. However, when the reactions are carried out in the absence of acetic anhydride, the yield of the products is drastically lowered to~20%. The characteristics of these products are given in table 2.6.

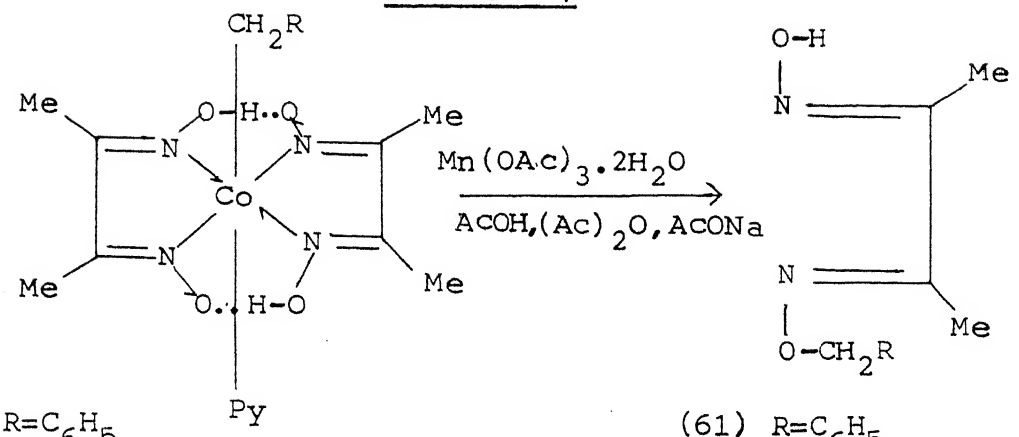
## 2.4.4 Discussion

In all the reactions discussed in this part of the chapter, benzyl ethers of dimethylglyoxime are the sole organic product isolated.

In view of our earlier observations in the halogenation of benzylcobaloximes where similar monoethers were obtained as a result of the decomposition of the intermediate oxidised species,[183] it is beyond doubt that Mn(III) acetate is acting more like an one electron oxidant rather than a $\dot{C}H_2COOH$ radical source as anticipated.

One electron oxidation of a number of organocobalt(III) complexes has been very successfully achieved both electrochemically[136] and chemically[135] (by suitable oxidants) and the resulting oxidised form is so unstable at ambient temperature that it is

Scheme 2.7




(12) R=$C_6H_5$

(13) R=4-$MeC_6H_4$

(14) R=4-$BrC_6H_4$

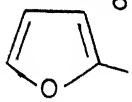
(15) R=4-$ClC_6H_4$

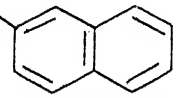
(16) R=4-$CNC_6H_4$

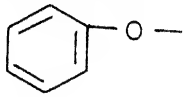
(17) R=4-$NO_2C_6H_4$

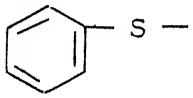
(18) R=4-$CHOC_6H_4$

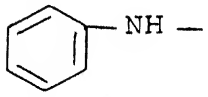
(19) R=4-$MeOC_6H_4$

(21) R= 

(24) R= 

(24a) R= 

(24b) 

(24c) 

(61) R=$C_6H_5$

(62) R=4-$MeC_6H_4$

(63) R=4-$BrC_6H_4$

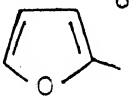
(64) R=4-$ClC_6H_4$

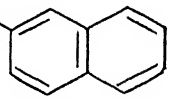
(65) R=4-$CNC_6H_4$

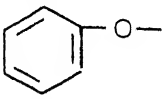
(66) R=4-$NO_2C_6H_4$

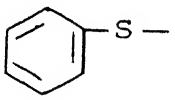
(87) R=4-$CHOC_6H_4$

(88) R=4-$MeOC_6H_4$

(89) R= 

(90) R= 

(90a) R= 

(90b) 

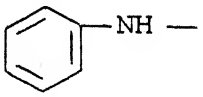
(90c) 

Table 2.6: Characteristics of HON=C(Me)-C(Me)=NO-$CH_2R$ (61-66), (87-90)

| Product Number | Yield (%) | Melting Point ($^oC$) | $^1H$ NMR Chemical shift(ppm)$\delta$ dmgH | $-CH_2$ | Aromatic | UV ($CH_3OH$) $\lambda$(nm) | Mass $(m/e)^+$ |
|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| (61) | 38 | 90-92 | 1.95 | 5.10 | 7.23 | - | - |
| (62) | 45 | 85 | 2.00<br>2.08 | 5.12 | 7.16 | 228 | 220(2%),105(100%) |
| *(63) | 56 | 100 | A 1.90,2.30<br>B 2.22,2.35 | 5.14<br>5.10 | 7.12,7.32<br>7.12,7.32 | 220 | 285(2%),170(100%)<br>283(2%),168(100%) |
| (64) | 52 | 98 | 1.90,2.30 | 5.16 | 7.20 | 226 | 239(1.5%),124(100% |
| (65) | 73 | 95 | 1.95,2.04 | 5.16 | 7.40,7.52 | 235 | 231(10%),116(100%) |
| (66) | 32 | 99 | A 2.05,2.35<br>B 2.18,2.22 | 5.35<br>5.10 | 7.50,8.20<br>7.50,8.20 | 217,230<br>260 | 250(60%),135(100%) |
| ++(87) | 50 | 93 | 2.25,2.28 | 5.18 | 7.52,7.90 | 236,273 | 234(6%),119(98%) |
| (88) | 41 | 71 | A 2.05,2.10<br>B 2.20,2.25 | 5.0<br>4.85 | 7.15,6.70 | 231 | 236(12%),121(50%) |

...contd.

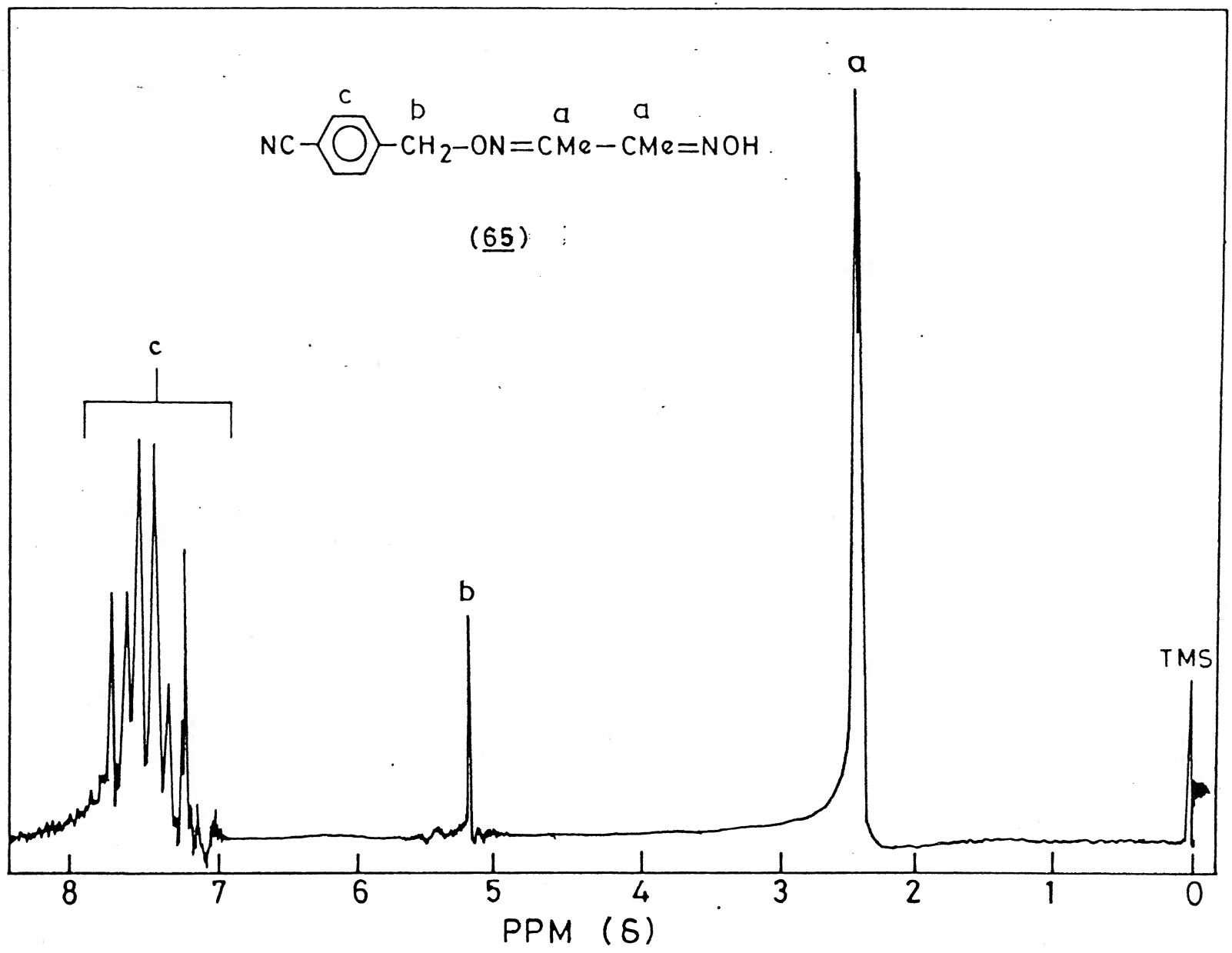
Table 2.6(contd.)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|
| (89) | 48 | 106 | A 2.28,2.32<br>B 2.18 | 5.14<br>5.27 | 6.40,7.58<br>6.40,7.58 | 222 | - |
| (90) | 40 | 115 | A 2.27,2.30<br>B 2.09,2.16 | 5.64<br>5.52 | 7.40,7.76,8.02<br>7.40,7.76,8.02 | 223 | 256(0.5%),141(100% |
| (90a) | 43 | 99 | 2.22,2.30 | 5.15 | 7.35 | 222 | - |
| (90b) | 42 | 101 | A 2.24,2.28<br>B 2.08,2.18 | 5.54<br>5.36 | 7.26,7.40<br>7.26,7.40 | 312 | 239(2%),122(100%) |
| (90c) | 40 | 74 | 2.24,2.27 | 5.20 | 7.30,7.46 | 228 | - |

* Two isomers were observed in some cases. The separation proved to be very difficult. However compound (24) was separated on a preparative TLC plate on silica gel using benzene/chloroform (1:1) as the eluents. The major component (90) (isomer A) has a m.p. 105°C and the minor (isomer B) has 75°C. The yield, melting point and uv presented in Table 2.6 refer to the mixture data. All the products gave satisfactory elemental analyses.

+ Values refer to $M^+$, (M-dmgH) but for (64) and (66), the values refer to $(M-H)^+$ and $(M-H-dmgH)^+$ and for (90b) it refers to $(M+H)^+$ and $(M-H-dmgH)^+$

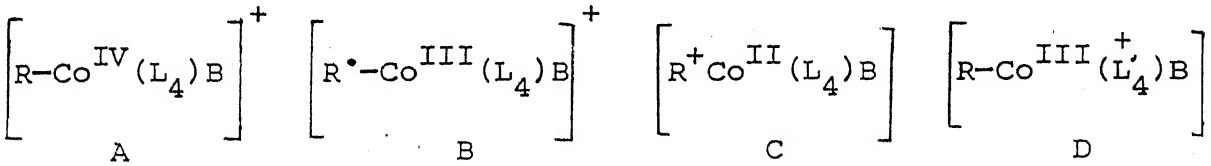
++ CHO appears at 10.0 δ.




$^1$H NMR SPECTRUM (90 MHz) OF (65)

detected only by cyclic voltametry and stop flow methods.[135,136] However at a lower temperature (−30 to −80°C) the life time is quite high and many studies including esr, have been reported in literature.[146,135,288] The solvent has a marked effect on the stability of the oxidised form, for example, strongly electron donating solvents like Py, DMF, DMSO accelerate the decomposition of this species whereas its life time is greatly reduced in the acidic medium. In order to know the decomposition mechanism of the oxidised species, an understanding of its structure and reactivity is necessary.

The structure of the oxidised form can be presented in terms of several formula, differing in location of the unpaired electron and/or in valency of the metal.



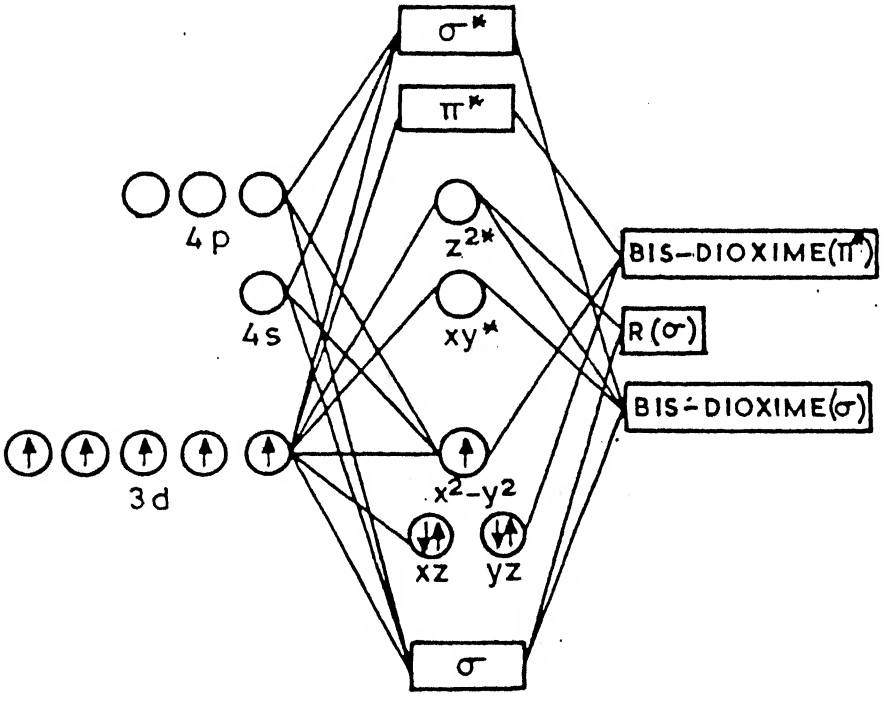

$L_4$ = bisbidentate or tetradentate ligand.

B = axial base ligand.

While A represents a complex with an usual Co–C covalent bond with +4 oxidation state on the metal, B and C can be viewed as complexes of organic free radical or carbonium ion with metal in +3 or +2 oxidation states, respectively. D is a cobalt(III) complex with a cation radical on the equational ligand ($L_4$). Though structure D

is predicted for organocobalt porphyrines[288] structure A seems to be more likely for schiff bases and organocobaloximes.[146]

ESR spectrum for organocobalt(IV) species reveals that the unpaired electron is localised predominantly on the metal.[145,181] The M.O. diagram is constructed by the $3dx^2-y^2$ orbital, interaction of the filled metal 'd' orbitals with the antibonding $\pi^*$ orbital of equatiorial dimethylglyoximato ligands.[181]




MO diagram for organobis(dioximato) cobalt (IV). Reproduced from ref. 181.

Three routes are possible by which organocobalt(IV) species can decompose in solution.

(i) Homolytic splitting: The decomposition of $R(Co^{IV})$ in solution has been found to involve homolytic splitting of the metal carbon bond.[138,289]

$$RCo^{IV}(L_4)B^+ \longrightarrow R^\bullet + Co^{III}(L_4)B^+$$

The possibility of such splitting can be postulated only from the formation of hydrocarbon products, i.e. RR (from self coupling of $R^\bullet$) and/or RH (from hydrogen abstraction by $R^\bullet$). The complete absence of bibenzyls and substituted toluenes in the present study rules out the possibility of such a process for the formation of the dimethylglyoxime monoethers.

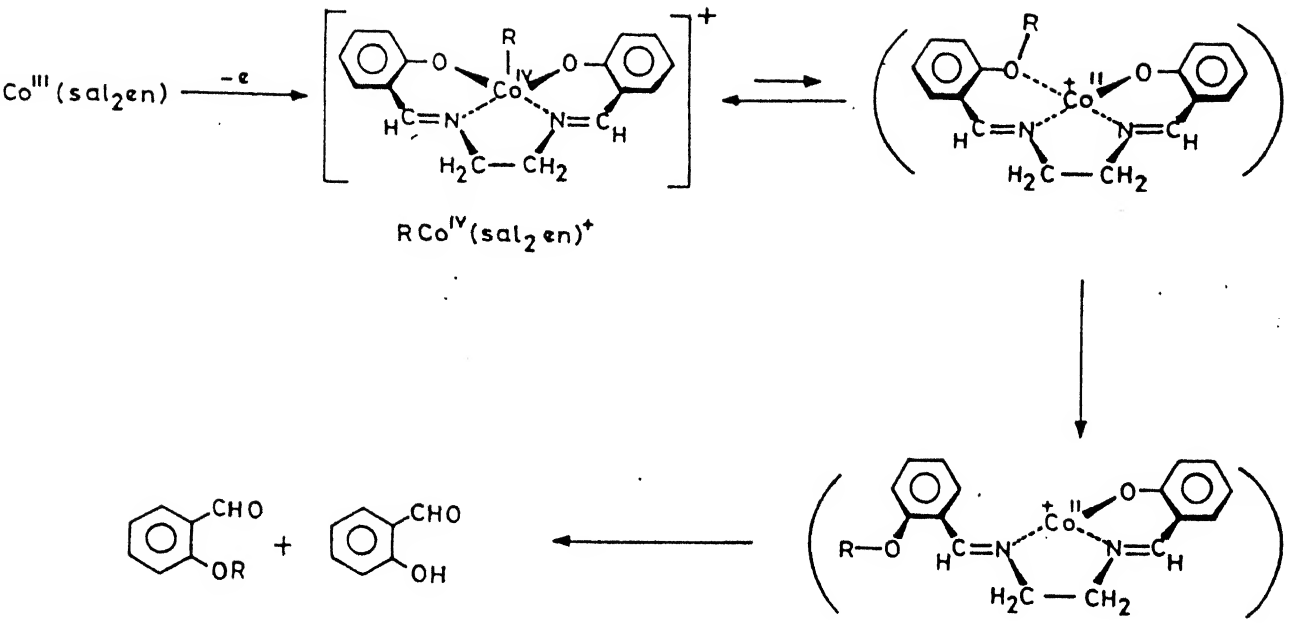
(ii) Nucleophilic substitution: The most characteristic reactions of organocobalt(IV) complexes are those of nucleophilic substitution at α carbon to metal.[136]

$$(R\text{-}Co^{IV})^+ + \ddot{N}u \longrightarrow R\text{-}Nu^+ + Co^{II}$$

For several schiff's bases and dimethylglyoximato complexes an $S_N2$ mechanism has been established with nucleophiles such as pyridine, water, $Cl^-$ etc.[138] The attack of $OAc^-$ ion on $R\text{-}Co^{IV}$ species in the present study is therefore expected. Considering the high concentration of acetate ion in the reaction medium, the complete absence of benzyl acetate is surprising. However, acetate

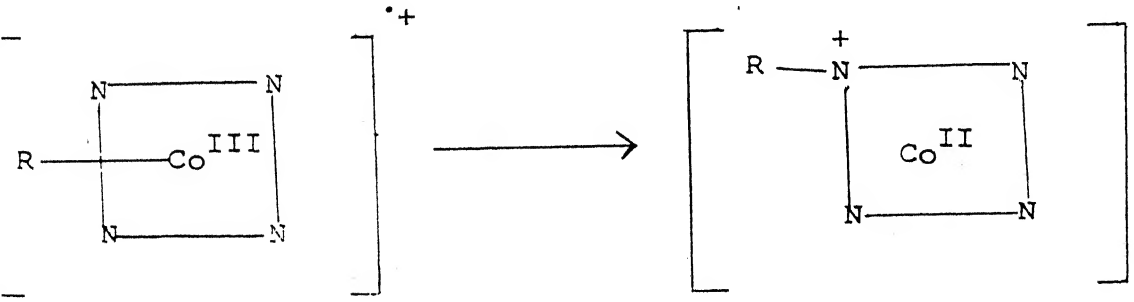
ion is much weaker as a nucleophile, any competition between nucleophilic displacement (a second order process) and monoether formation (probably a first order process) will favour the formation of the latter. From a recent study in our laboratory it has been observed[183] that, when the bromination of 4-nitrobenzylcabaloxime is carried out in the presence of $Cl^-$, the amount of 4-nitrobenzyl chloride formed is quite small because of the poor nucleophilicity of $Cl^-$. (The absence of benzylacetate in these reaction can be explained in view of the fact that pearson nucleophilicity of $OAc^-$ is much less than $Cl^-$).

(iii) Intramolecular decomposition: Most of the organocobalt(IV) complexes having Schiff's bases undergo nucleophilic displacement at carbon just like the corresponding dioximato complexes. However kinetic data[138] is consistent with $S_N1$ or $S_Ni$ mechanism. A clear cut example of $S_Ni$ mechanism involves transfer of R group from the metal to adjacent donor atom of the chelating ligand is given in Scheme 2.8.[142] This process is always in a direct competition with the $S_N1$ process.



Scheme 2.8 Electrooxidation and decomposition of alkylcobalt(III)chelate with schiff base $(SalH)_2$ en [142]

Similar inner sphere transfer of R group from the metal to the adjacent donor atom also occurs in $RCo^{IV}$-porphyrin complexes.[139]



In view of the fact that $S_Ni$ reactions are not uncommon in such complexes and the observed products in the present study are only the alkylated products of the equatorial dimethylglyoxime ligand, it is therefore possible that such a $S_Ni$ process is responsible for its formation. However, the transfer of R group may occur either as a nucleophilic displacement of $Co^{II}$ by the dimethylglyoxime anion ($S_N2$) or as a homolytic displacement of $Co^{III}$ by the dimethylglyoxime radical ($S_H2$).[261c] It is, however, very difficult to distinguish between these two processes, though $S_H2$ mechanism has been preferred by earlier workers.[173,261]

# CHAPTER 3

# MOLECULAR INSERTIONS INTO Co–C BOND IN ORGANOCOBALOXIMES

## 3.1 Background

Organocobaloximes are the accepted best model compounds for Vitamin $B_{12}$ coenzyme. Because of their tremendous usefulness in mediating different types of organometallic reactions, the synthesis of new organocobaloximes with new or modified structural features continues to be a fascinating area in the organocobaloxime chemistry.[40b] This is moreso because of the yet incomplete understanding of structure vs Co–C bond reactivity in such systems. Insertion of small molecules into metal carbon bond may become a valuable tool in interpreting such relationship chemically, for example, among the factors that influence the reactivity towards oxygen include the relative strength of the metal carbon and metal oxygen bond, the Lewis acidity (or complexing ability) of the organometallic complex and even the electronetativity of the metal.[295]

Several papers have been published on the ability of small molecules like $O_2$, $SO_2$ and S to enter into the Co-C bond in organocobaloximes,[33,35,36] however, all attempts to insert CO, $CO_2$, $CS_2$ etc into Co-C bond have failed. Oxygen insertion affords the peroxy complexes whereas the $SO_2$ insertion forms s-sulphinato or o-sulphinato complexes. Many excellent review articles have been published on these topics.[290-292,295,296] Inspite of the fact that a large amount of work has already been done on these reactions[290-298] a continued interest in this field exists in view of a) their emerging synthetic prospects, for example, recently the dioxy cobalt complexes have played a potential role in mediating many interesting chemical transformations, catalytic or otherwise.[192,299] b) their diverse mechanistic features, for example, no unified mechanism has emerged so far in the $SO_2$ insertion reactions inspite of many kinetic and streochemical studies.[290-298] Recently, both chain[173a] and non chain[189b] mechanism have been pointed out for such a reaction in organocobaloximes casting a doubt about the true insertion nature of these reactions. c) the ease with which these reactions undergo.

In light of the above discussions, we have undertaken the project which aims at the synthesis of new organocobaloximes and to study their behaviour towards molecular oxygen and sulphur dioxide under variable reaction conditions. The kinetic studies on the oxygen insertions have been carried out to establish the

mechanism of these reactions. An attempt has also been made to look into the true insertion nature of the sulphur dioxide reactions.+

## 3.2 Experimental

The general experimental procedure including details of solvents, chromatography, physical measurements and instrumentation are same as those described earlier in chapter 2, sec. 2.2. The following additional features are noteworthy.

### Gases:

Sulphur dioxide gas was generated by the treatment of solid sodium sulphite with dil. sulphuric acid. Ammonia and oxygen were used as such from the cylinder.

### Starting materials

Cyclohexanone, hydroxylaminehydrochloride, salicyaldehyde, chloroacetic acid, carbondisulphide, benzaldehyde, nitrobenzene, iodine, thianaphthene, dimethylsulfoxide, sodiumhydride, quinoline, morpholine, piperidine, γ-picoline, lithium aluminium hydride, were commercial materials and were used as such in most cases.

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+A part of the work was initiated by Dr. Sujit Roy.

## 3.2.1 Synthesis of organic precursors

The preparative routes for the organic precursors are outlined in scheme 3.1 and are described below.

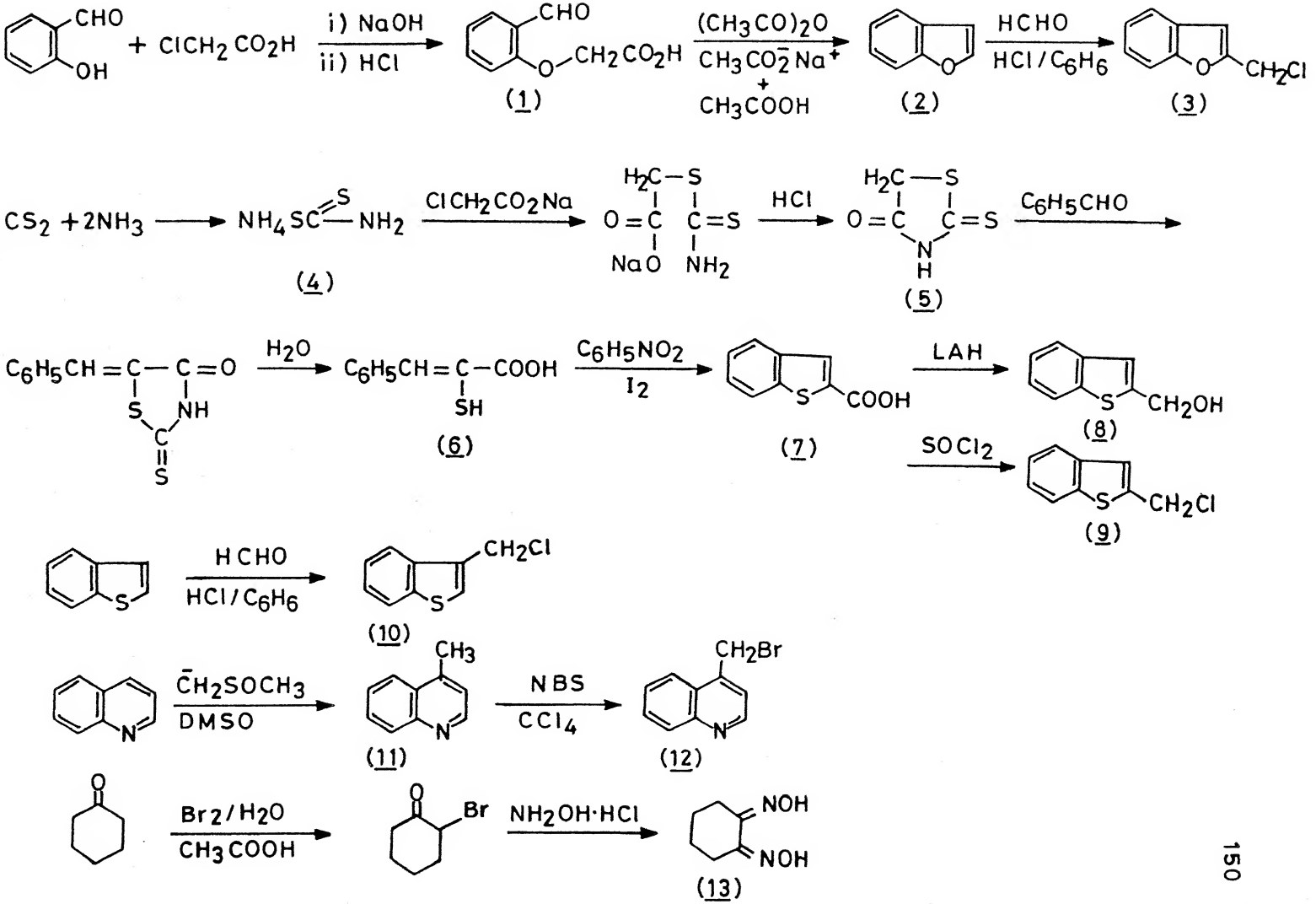
### Preparation of o-Formylphenoxy acetic acid (1)[266]

A solution of sodium hydroxide (13.3 g in 100 ml water) was slowly added with stirring to a mixture of salicylaldehyde (17.5 ml), chloroacetic acid (15.7 g) and water (125 ml). The solution was heated to reflux for 3 hr, cooled and acidified with conc. hydrochloric acid (30 ml) and steam distilled to remove unreacted salicylaldehyde. The residual liquid on cooling afforded colourless crystals. Yield (12 g, 63%), m.p. 131°C (lit.[266] m.p. 132-133°C).

### Preparation of Benzofuran (2)[266]

A mixture of o-formylphenoxy acetic acid (10 g), anhydrous sodium acetate (20 g), acetic anhydride (50 ml) and glacial acetic acid (50 ml) was heated to reflux for 8 hr. The light brown solution was poured into iced water (~300 ml) with occassional stirring. The solution was extracted with three 70 ml portion of ether. The ether extract was washed with 5% aqueous sodium hydroxide solution followed by water. Evaporation of the solvent followed by distillation gave the product (3.1 g, 89%), b.p. 52°C/5 mm (lit.[266] b.p. 170-172°C).

## Scheme 3.1


CHO
OH
+ ClCH2CO2H
i) NaOH
ii) HCl
CH2CO2H
(1)
(CH3CO)2O
CH3CO2⁻Na⁺
CH3COOH
(2)
HCHO
HCl/C6H6
CH2Cl
(3)
CS2 +2NH3
NH4SC(=S)NH2
(4)
ClCH2CO2Na
HCl
C6H5CHO
(5)
H2O
C6H5CH=C(S)-COOH
(6)
C6H5NO2
I2
COOH
(7)
LAH
CH2OH
(8)
SOCl2
CH2Cl
(9)
HCHO
HCl/C6H6
CH2Cl
(10)
CH3
(11)
C̄H2SOCH3
DMSO
NBS
CCl4
CH2Br
(12)
Br2/H2O
CH3COOH
Br
NH2OH·HCl
NOH
NOH
(13)

Preparation of 2-chloromethyl benzofuran (3)[300]

Hydrogen chloride gas was passed for ten minutes through a stirred solution of formaldehyde (2.2 g), benzene (10 ml) and conc. hydrochloric acid (13 ml). Benzofuran (3.0 g) was added to this solution and stirring was continued at room temperature for 2.5 hr. After the addition of water, the organic layer was separated and the aqueous layer was extracted with benzene. The combined organic layer was washed with water, saturated sodium-bicarbonate solution and water. The organic layer was dried over anhyd. calcium chloride. Evaporation of solvent and distillation under reduced pressure gave the product (2.2 g, 52%), b.p. 93°C/2 mm (lit.[300] b.p. 107-110°/5 mm).

Preparation of ammonium dithiocarbamate (4)[270]

Ammonium dithiocarbamate was prepared from ammonia, 95% ethanol and carbondisulphide at 0°C according to procedure outlined in organic synthesis (yield 21.0 g).

Preparation of Rhodanine (5)[270]

Freshly prepared ammonium dithiocarbamate (20.0 g) was added slowly to a solution of chloroacetic acid at 0°C. After all the dithiocarbamate was added, the ice bath was removed and the solution was allowed to stand for 30 minutes during which the colour of the solution turned light yellow. The solution was

poured slowly with stirring into 6N hydrochloric acid (100 ml) in hot condition maintaining the temperature at 95°C. On cooling the Rhodanine crystals were separated. (yield 19.5 g, 80%), m.p. 166°C (lit.[270] m.p. 165-168°C).

Preparation of α-mercapto acrylic acid (6)[301]

Rhodanine (13.3 g) was treated with equimolar amount of benzaldehyde (10.6 g) and 3 molar equivalents of anhydrous sodium acetate in boiling acetic acid to give α-mercapto acrylic acid (10.8 g), m.p. 133°C (lit.[301] m.p. 133-134°C).

Preparation of thianaphthene-2-carboxylic acid (7)[302]

Iodine (24.0 g) was dissolved in nitrobenzene (180 ml) and heated to boiling. α-Mercapto acrylic acid (2.4 g) was added to this solution and the mixture was stirred for one minute and then it was immediately cooled. The product so formed was extracted in dil. sodium hydroxide solution. The alkaline solution was treated with sodium bisulphite and acidified with hydrochloric acid. The light brown crystals were separated and further recrystallised from chloroform (yield 1.6 g, m.p. 240° (lit.[302] m.p. 240-241°C).

Preparation of Thianaphthene-2-methanol (8)[303]

Lithium aluminium hydride (0.5 g in 50 ml of dry ether) was placed in a soxlet extraction unit. Thianaphthene-2-carboxylic acid (1.6 g) was placed in the thimble and the compound was extracted by refluxing ether for 24 hrs. A careful workup by addition of water, sulphuric acid etc. gave thianaphthene-2-methanol (1.5 g, 98%), b.p. 142°C/5 mm (lit.[303] b.p. 123-125°C/1.5 mm).

Preparation of 2-chloromethylthianaphthene (9)[303]

A mixture of thianaphthene-2-methanol (1.5 g) and thionyl chloride (1.4 g) was refluxed for 2 hr. The distillation under reduced pressure afforded the product 2-chloromethylthianaphthene (1.3 g, 79%), b.p. 126°C/2 mm (lit.[303] b.p. 145°C/5 mm).

Preparation of 3-chloromethylthianaphthene (10)[304]

Thianaphthene (3.0 g) was chloromethylated by conc. hydrochloric acid (2.2 ml), 37% formaldehyde solution (2.2 g). A stream of hydrogen chloride was passed at room temperature with stirring. The temperature was raised to 65°C and hydrogen chloride gas was passed slowly for 1 hr. The usual aqueous workup and distillation of crude product afforded the pure 3-chloromethylthianaphthene (2.8 g, 70%), b.p. 138°C/5 mm (lit.[304] b.p. 149-156°C/11 mm).

Preparation of 4-methylquinoline (11)[305]

Quinoline (10.0 g) was added to a freshly prepared solution of dimethylsulphinyl carbanion (prepared from dry and degassed dimethylsulphoxide (12.5 ml) and sodiumhydride (0.5 g) at 65-70°C). The mixture was stirred at 60-70°C for 6 hr. The aqueous workup and distillation gave 4-methylquinoline (3.1 g, 28%), b.p. 117°C/5 mm (lit.[305] b.p. 133°C/11 mm).

Preparation of 4-bromomethylquinoline (12)[306]

4-Methylquinoline (3.0g) was brominated with N-bromosuccinimide (3.7 g) in carbon tetrachloride (46 ml). After usual workup, and recrystallisation gave 4-bromomethylquinoline (2.8 g, 60%), m.p. 64°C (lit.[306] m.p. 65°C).

Preparation of 1,2-cyclohexanedione dioxime (13)[307]

2-Bromocyclohexanone (32.0 g), prepared from bromine (40.0 g) cyclohexanone (25.0 g), acetic acid (40 ml) and water (60 ml) at 45-50°C, was added dropwise into a refluxing solution of hydroxylamine hydrochloride (57.0 g) and sodium acetate trihydrate (114.0 g) in 200 ml methanol water (1:1, v/v) mixture. Refluxing was continued for another one hr. after which 100 ml of solvent was distilled out from the mixture. The residual solution was cooled to 0°C to give crude dioxime (13) which was recrystallised from water as colour less needless (7.0 g, 22%), m.p. 187°C (lit.[307] m.p.186-187°C).

### 3.2.2 Synthesis of Organocobaloximes

**Preparation of 2-thienylmethyl (14), 3-thienylmethyl (15), furfuryl (16), 3-furylmethyl (17), 2-benzofurylmethyl (18), 2-thianaphthylmethyl (19), 3-thianaphthylmethyl (20) and 4-quinolylmethyl (21) bis(dimethylglyoximato)pyridine cobalt(III) complexes**

The preparation of organocobaloximes (14-17)* have earlier been described in chapter 2 (p. 91 ). Organocobaloximes (18-21) were prepared by the same procedure (Scheme 3.2).

**Preparation of 2-thienylmethyl (22), 3-thienylmethyl (23), furfuryl (24), 3-furylmethyl (25), 2-benzofurylmethyl (26), 2-thianaphthylmethyl (27) and 3-thianaphthylmethyl (28) bis-(cyclohexane glyoxime)pyridine cobalt(III) complexes**

The general procedure followed was exactly similar to the method described earlier on p. 91 for the synthesis of (14-17) except that cyclohexane 1,2 dioxime (13) was used instead of dimethylglyoxime in same molar ratio (Scheme 3.2).

---

* The organocobaloximes (14-17) have been described earlier in second chapter (p. 91 ). However, the numbering in this chapter for these cobaloximes is done for convenience only and it differs from the numbering in the second chapter.

Preparation of 2-thienylmethyl bis(dimethylglyoximato) γ picolin (29), morpholine (30) and piperidine (31) cobalt(III) complexes

The general method adopted was similar to the method described on p. 91 except that the bases γ picoline, morpholine and piperidine were used instead of pyridine in same molar ratio.

Preparation of benzyl (32), 4-methylbenzyl (33), 4-chlorobenzyl (34), 4-cyanobenzyl (35) and 4-nitrobenzyl (36) cobaloximes

The synthesis of these cobaloximes has been described earlier in chapter 2 p. 91 . However, new numbers have been given for convenience only The spectral characteristics of the cobaloximes (14-28) and (29-31) are given in table 3.1 and 3.5 respectively.

3.2.3 Sulphurdioxide insertion into organocobaloximes (14-25) and (32-37)

R.1 Under photochemical conditions

In a typical experiment, a solution of the organocobaloxime (0.2 mmol) in dichloromethane (30 ml) was purged with a stream of dry A.R. nitrogen gas to eliminate trace of oxygen present in it. Sulphur dioxide was bubbled through the solution under a positive pressure of nitrogen. This was achieved by allowing nitrogen gas to drive through the sulphur dioxide generator. The solution was irradiated at $0^{\circ}$- $(-10)^{\circ}C$ with two 200 W tungsten lamps at approximately 5 cm apart. Most of the reactions were complete within

Scheme 3.2

$Co^{I}(dmgH)_2Py \xrightarrow{RX} RCo^{III}(dmgH)_2Py$

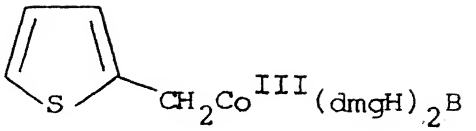
R =

(14) 2-Thienylmethyl
(15) 3-Thienylmethyl
(16) Furfuryl
(17) 3-Furylmethyl
(18) 2-Benzofurylmethyl
(19) 2-Thianaphthylmethyl
(20) 3-Thianaphthylmethyl
(21) 4-Quinolylmethyl
(32) Benzyl
(33) 4-Methylbenzyl
(34) 4-Chlorobenzyl
(35) 4-Cyanobenzyl
(36) 4-Nitrobenzyl

$Co^{I}(chgH)_2Py \xrightarrow{RX} RCo^{III}(chgH)_2Py$

R =

(22) 2-Thienylmethyl
(23) 3-Thienylmethyl
(24) Furfuryl
(25) 3-Furylmethyl
(26) 2-Benzofurylmethyl
(27) 2-Thianaphthylmethyl
(28) 3-Thianaphthylmethyl

$Co^{I}(dmgH)_2B \xrightarrow{\text{2-Chloromethylthiophene}}$ 


(29) B = γ Picoline
(30) B = Morpholine
(31) B = Piperidine

2 hr. with wet sulphur dioxide. However,with dry sulphur dioxide+ reactions took longer time (4-6 hr.). The reaction was monitored by TLC on silica gel using ethyl acetate as eluent. The solution was concentrated in vacuo at room temperature and poured into 30 ml of petroleum ether(40-60°). The precipitated solid was filtered and dried in vacuo. However,no reaction occured in case of (21). The yields of the products were nearly quantitative.

R.2 Under thermal conditions

The procedure adopted was similar to one described under R.1 except that sulphur dioxide was bubbled through the refluxing (dichloromethane) solution of organocobaloxime in dark. However no insertion took place and the starting material was recovered after a few hours.

R.3 Reaction of sulphur dioxide with a mixture of two cobaloximes

In a typical experiment, 2-thienylmethyl bis(dimethylglyoximato)pyridine cobalt(III) (14) (0.2 mmol) and furfuryl bis(cyclohexaneglyoximato)pyridine cobalt(III) (24) (0.2 mmol) were taken

+ By dry sulphur dioxide we mean that, the sulphur dioxide after generation from sodium sulphite and dil. sulphuric acid was passed through the traps of sulphuric acid and anhydrous calcium chloride and the solution of organocobaloxime was kept over molecular seives during the reaction.

in dichloromethane (50 ml) and the reaction was carried out as described under R.1 p. 156 . On workup of the reaction, $^{1}H$ NMR spectrum of the total mixture showed the presence of four products which were identified by comparison with corresponding spectra of authentic samples. All attempts to separate these products by chromatography failed.

A similar reaction with a mixture of furfuryl bis(dimethyl-glyoximato)pyridine cobalt(III) (16) and 2-thienylmethyl bis-(cyclohexane glyoximato)pyridine cobalt(III) (22) also resulted in the formation of four products.

### 3.2.4 Oxygen insertion into organocobaloximes (14-31)

R.4 Under photochemical conditions

The general procedure was exactly similar to the method R.1 p. 156 except that oxygen gas was bubbled through the solution instead of sulphurdioxide. The reactions were complete within 1 hr. and the yields were quantitative in all cases, however no insertion was observed in case of (21).

R.5 Under thermal conditions

A similar procedure as that of R.1 was adopted except that the solution of organocobaloxime in dichloromethane was heated to reflux in dark. No insertion reaction occured within 20 hr.,

however, after 40 hr , the initial cobaloxime was consumed (TLC inference only) and more than one product was obtained. The products were separated on a preparative TLC plate using a mixture of dichloromethane–acetone (3:1, v/v).

R.6 Kinetics of oxygen insertion under photochemical conditions at room temperature (30°C)

The following general procedure was used.

0.0232 g of 2-thienylmethyl cobaloxime ($10^{-3}$M) was dissolved in 50 ml of 95% ethanol. Oxygen was passed through the solution at a fixed pressure while it was irradiated by 200 W tungsten lamp at room temperature (30°C). The lamp was placed at about 5 cm away from the reaction vessel. The progress of reaction was monitored by noting absorbance at a fixed wave length (450 nm) at regular intervals of time.

In another experiment, a solution of the organocobaloximes ($10^{-3}$M) in 95% ethanol was taken in a spectrophotometric cell and was stoppered. The solution was irradiated by 200 W tungsten lamp at room temperature (30°C). The progress of reaction was monitored as described above.

# RESULTS AND DISCUSSION

## $SO_2$ INSERTION

## 3.3 Results and Discussion

Furfuryl cobaloxime (16) reacts under photolytic conditions with $SO_2$ gas (wet or dry)* in less than one hr. at 0°C to give the corresponding inserted product (16a) in nearly quantitative yield. The I.R. spectrum shows it to be a S-sulphinato complex. Similar reactions of 2-thienylmethyl, 3-thienylmethyl and 3-furylmethyl cobaloximes (14, 15 and 17 respectively) with $SO_2$ gas under identical conditions form the corresponding inserted products (14a, 15a and 17a respectively) in nearly quantitative yield. Similarly, the reactions of organobis(cyclohexaneglyoxime)pyridine cobalt(III) complexes (22-25) with $SO_2$ gas proceed slowly (~1.5 hr.) but smoothly and the corresponding s-sulphinato inserted products (22a-25a) are formed in nearly quantitative yield. On the other hand, the reaction of the corresponding benzoanalogues (18-20) with $SO_2$ gas are not clean and a side product, insoluble in most of the common organic solvents, is formed in each case besides the required inserted product. The amount of the insoluble product formed is increased by about 20% when the reaction is carried out with wet $SO_2$. Similar observations are made in the reaction of benzyl, parasubstituted benzyl (32-36) and thiophenoxy methyl (37)+ cobaloximes with $SO_2$ gas. In case of the reaction of benzyl cobaloxime (32) with liq. $SO_2$ in a sealed tube

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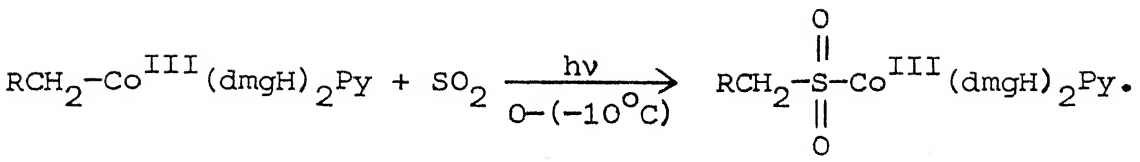
*Dry and wet $SO_2$ has been defined on page 158.

+Cobaloxime (37) was available from a different study in our lab.

Scheme 3.3




$RCH_2$ =

(14) 2-Thienylmethyl

(15) 3-Thienylmethyl

(16) Furfuryl

(17) 3-Furylmethyl

(18) 2-Benzofurylmethyl

(19) 2-Thianaphthylmethyl

(20) 3-Thianaphthylmethyl

(32) Benzyl

(33) 4-Methylbenzyl

(34) 4-Chlorobenzyl

(35) 4-Cyanobenzyl

(36) 4-Nitrobenzyl

(37) Thiophenoxymethyl

(14a) 2-Thienylmethyl

(15a) 3-Thienylmethyl

(16a) Furfuryl

(17a) 3-Furylmethyl

(18a) 2-Benzofurylmethyl

(19a) 2-Thianaphthylmethyl

(20a) 3-Thianaphthylmethyl

(32a) Benzyl

(33a) 4-Methylbenzyl

(34a) 4-Chlorobenzyl

(35a) 4-Cyanobenzyl

(36a) 4-Nitrobenzyl

(37a) Thiophenoxymethyl

Scheme 3.4

$$RCH_2\text{-}Co^{III}(chgH)_2Py + SO_2 \xrightarrow[0^oC]{h\nu} RCH_2\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}Co^{III}(chgH)_2Py$$

$RCH_2$- =

(22) 2-Thienylmethyl (22a) 2-Thienylmethyl

(23) 3-Thienylmethyl (23a) 3-Thienylmethyl

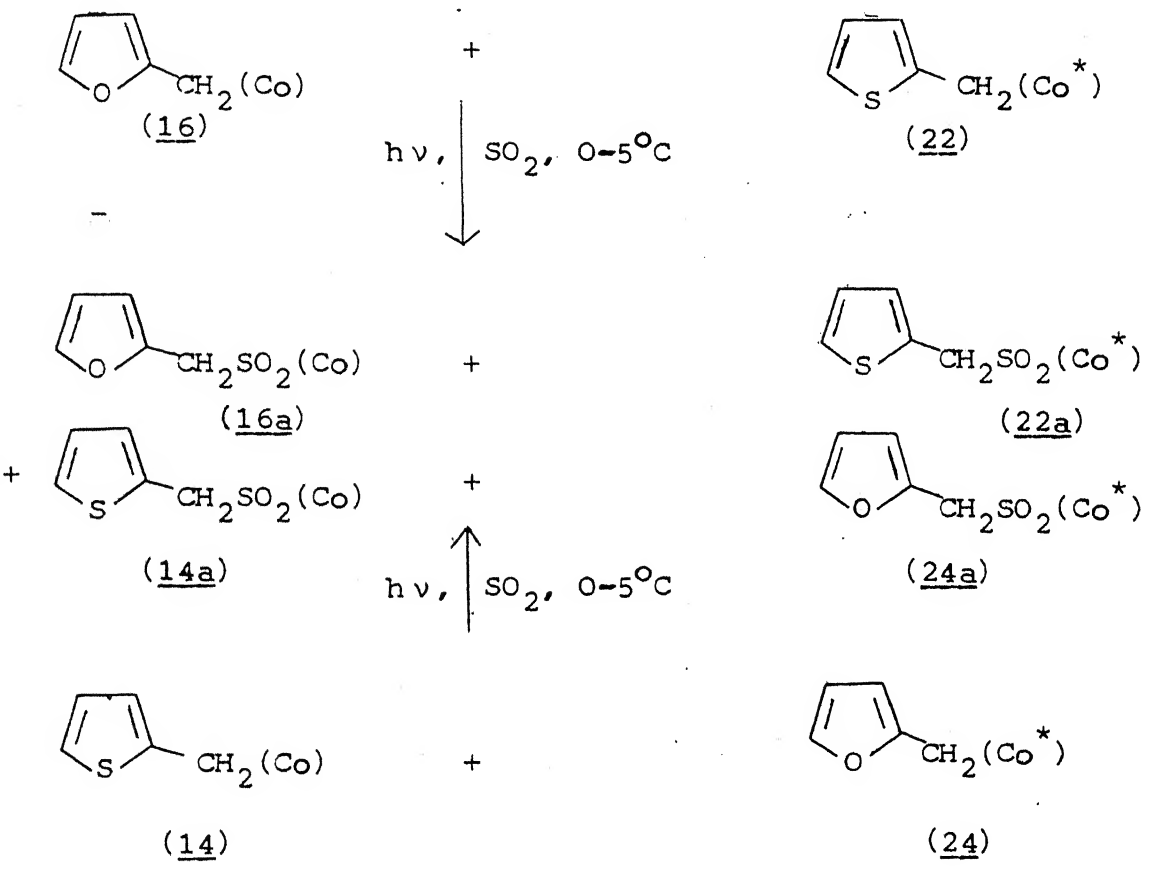
(24) Furfuryl (24a) Furfuryl

(25) 3-Furylmethyl (25a) 3-Furylmethyl

at room temperature, the reaction is much cleaner and sulphur-dioxide inserted product (32a) is the exclusive organometallic product formed. However, the same reaction with 2-thianaphthyl methyl cobaloxime (19) forms the same mixture of products as obtained with sulphur dioxide gas. The $^1H$ NMR spectrum of the reaction mixture shows the presence of paramagnetic impurities which are removed by washing with water. 4-Quinolylmethyl cobaloxime (21) does not undergo insertion under any conditions, photochemical or thermal.

When an equimolar mixture of (16) and (22) is reacted with $SO_2$ gas under the above conditions, besides the expected products (16a and 22a), two more new products (14a and 24a) are observed to be formed in the $^1H$ NMR spectrum (fig. ) of the mixture. Similar reaction of a mixture of (14) and (24) gives a mixture of four products i.e. (14a), (24a), (16a) and (22a). All attempts to separate these inserted products by chromatography (various

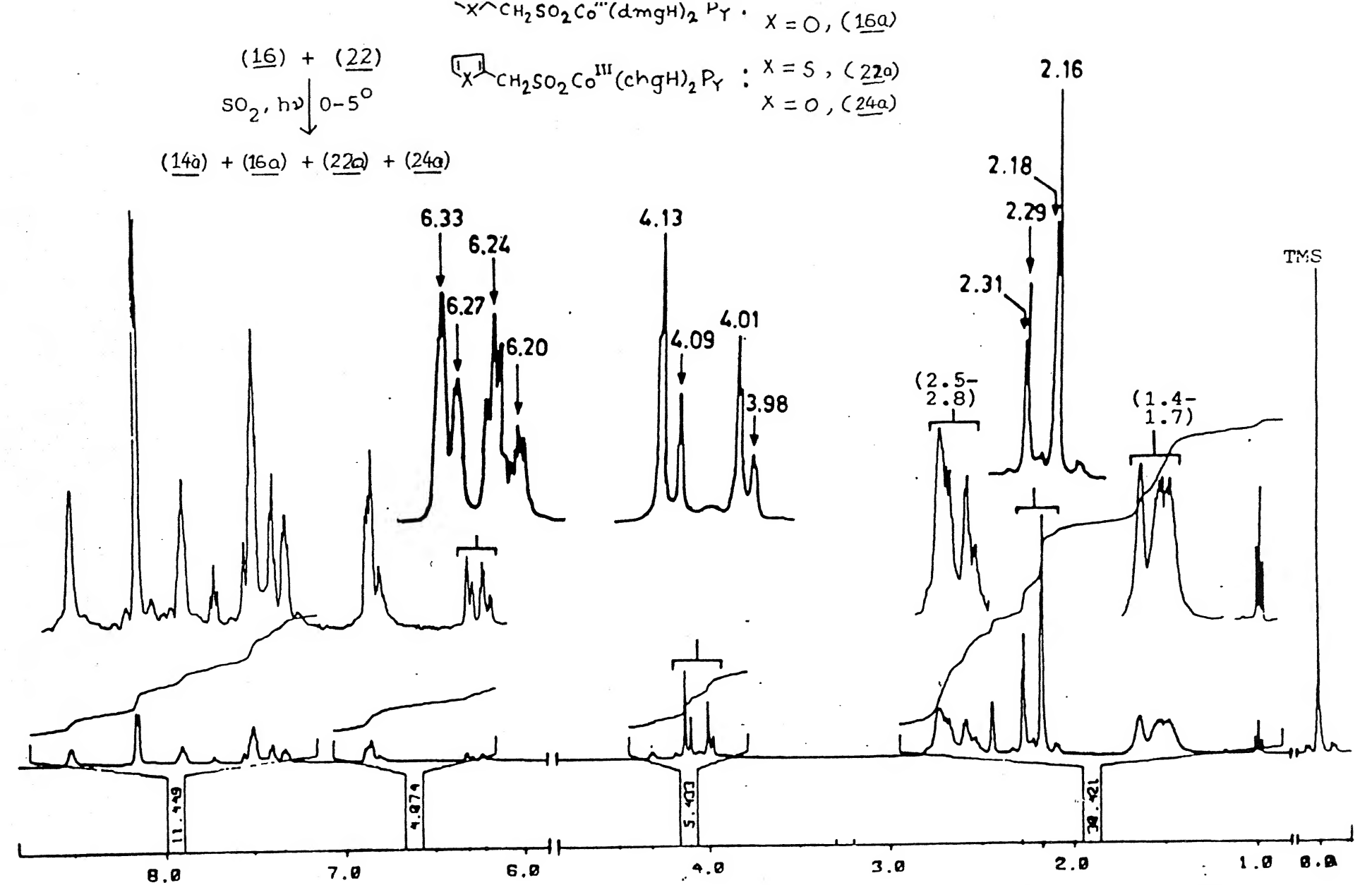
solvent system tried) or by partial recrystallisation failed. The characteristics of all the products are given in Table 3.2 and 3.3.




(Co) = $Co^{III}(dmgH)_2Py$; (Co*) = $Co^{III}(chgH)_2Py$

Furthermore, the following observations are made from the independent experiments.

1. No insertion product is formed at $0^{o}C$ without irradiation.
2. All the reactions show concentration dependent induction time. However, once the induction time is over, the reaction proceeds to completion without any further irradiation.




$^1$H NMR Spectrum (400 MHz) δ(ppm) of the products from the reaction of $SO_2$ with (16) + (22)

Table 3.1: Spectral characteristics of organocobaloximes $RCH_2Co^{III}(L_2)Py$ (14-28)*

| Compound No | $RCH_2$ | L | $^1H$ NMR Chemical shift (δ): $CDCl_3$ | | | Pyridine | | | $\lambda^{nm}_{CH_3OH}(\log\varepsilon)$ |
|---|---|---|---|---|---|---|---|---|---|
| | | | Aromatic | $CH_2$ | dmgH/chgH | α | β | ν | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| (14) | 2-Thienylmethyl | dmgH | 6.65,7.00 | 3.00 | 2.05 | 7.20 | 7.65 | 8.50 | 385(3.42),281(3.12), 240(3.49) |
| (15) | 3-Thienylmethyl | '' | 6.65,7.20 | 2.85 | 2.00,2.10 | 7.30 | 7.70 | 8.50 | 359(3.20),277(3.21), 239(3.60) |
| (16) | Furfuryl | '' | 6.00,7.40 | 2.40 | 2.00 | 7.30 | 7.75 | 8.60 | 383(3.39),284(3.18), 239(3.58) |
| (17) | 3-Furylmethyl | '' | 6.00,7.12 | 2.55 | 2.00,2.10 | 7.15 | 7.75 | 8.42 | 348(3.22),286(3.31), 238(3.56) |
| (18) | 2-Benzofurylmethyl | '' | 6.39,7.06, 7.18,7.44 | 2.76 | 1.97 | 7.30 | 7.75 | 8.54 | 298(4.68),282(4.71), 242(5.0) |
| (19) | 2-Thianaphthylmethyl | '' | 6.94,7.22, 7.60 | 3.02 | 2.00 | 7.30 | 7.70 | 8.56 | 300(4.00),260(4.41), 257(4.48),249(4.46), 242(4.45) |
| (20) | 3-Thianaphthylmethyl | '' | 7.04-7.80 | 3.04 | 1.95,1.85 | a | a | 8.46 | 295(3.76),260(4.26), 257(4.34),249(4.30), 242(4.28) |
| (21) | 4-Quinolylmethyl | '' | 7.10-8.32 | 2.46 | 2.24 | 7.35 | 7.70 | 8.50 | 288(4.60),237(4.99) |

...contd.

Table 3.1(contd.)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| (22) | 2-Thienylmethyl | chgH | 6.72,7.05 | 3.04 | 1.36-1.80, 2.40-2.70 | 7.25 | 7.64 | 8.48 | 365(2.91),315(3.13), 247(3.57) |
| (23) | 3-Thienylmethyl | '' | 6.74,6.98 | 2.82 | 1.60, 1.90-2.10 | 7.28 | 7.70 | 8.56 | 463(2.94),315(4.04), 243(4.46) |
| (24) | Furfuryl | '' | 6.06 | 3.54 | 1.40-1.98, 2.55-2.75 | 7.18 | 7.65 | 8.50 | 308(3.67),245(3.95) |
| (25) | 3-Furylmethyl | '' | 6.13, 7.16-7.49 | 2.60 | 1.30-1.70, 2.30-2.90 | a | 7.73 | 8.59 | 458(2.98),345(3.61), 235(4.35) |
| (26) | 2-Benzofurylmethyl | '' | 6.40,7.08, 7.18,7.28, 7.42 | 2.80 | 1.28-1.84, 2.36-2.58 | 7.28 | 7.77 | 8.54 | 305(4.11),280(4.17), 218(5.10) |
| (27) | 2-Thianaphthylmethyl | '' | 6.98,7.20, 7.28,7.62 | 3.06 | 1.16-1.86, 2.30-2.64 | 7.31 | 7.72 | 8.56 | 303(4.32),253(4.56), 228(4.59) |
| (28) | 3-Thianaphthylmethyl | '' | 7.31-7.60, 7.69-8.0 | 3.13 | 1.00-1.30, 2.35-2.63 | a | a | 8.59 | 390(.256),293(1.00), 235(.26),213(.45) |

a , obscured.

* Spectral characteristics of benzyl cobaloximes (32-37) have already appeared in chapter 2, p.96.

Table 3.2(contd.)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|
| (32a) | Benzyl | 7.11–7.52 | 4.18 | 2.30 | a | 7.78 | 8.50 | 331, 322 |
| (33a) | 4-Methylbenzyl | 7.1 –7.50 | 4.15 | 2.35* | a | 7.75 | 8.50 | 337, 244, 215 |
| (34a) | 4-Chlorobenzyl | 7.10–7.65 | 4.10 | 2.33 | a | 7.85 | 8.45 | 331, 244, 218 |
| (35a) | 4-Cyanobenzyl | 7.13–7.75<br>7.89 | 4.13 | 2.24 | a | a | 8.20 | 325, 253 |
| (36a) | 4-Nitrobenzyl | 7.20–7.60<br>8.0 –8.30 | 4.24 | 2.35 | a | a | 8.45 | 329, 248 |
| (37a) | Thiopenoxymethyl | 7.02–7.97 | 4.26 | 2.29 | a | a | 8.36 | 362, 300, 244 |

+ : For all compounds characteristic IR(KBr) absorption frequencies for ($Co-SO_2$) linkage appear at $\nu_{sym}$ (1060–1070) and $\nu_{asym}$ (1220–1230) $cm^{-1}$.

a : obscured.

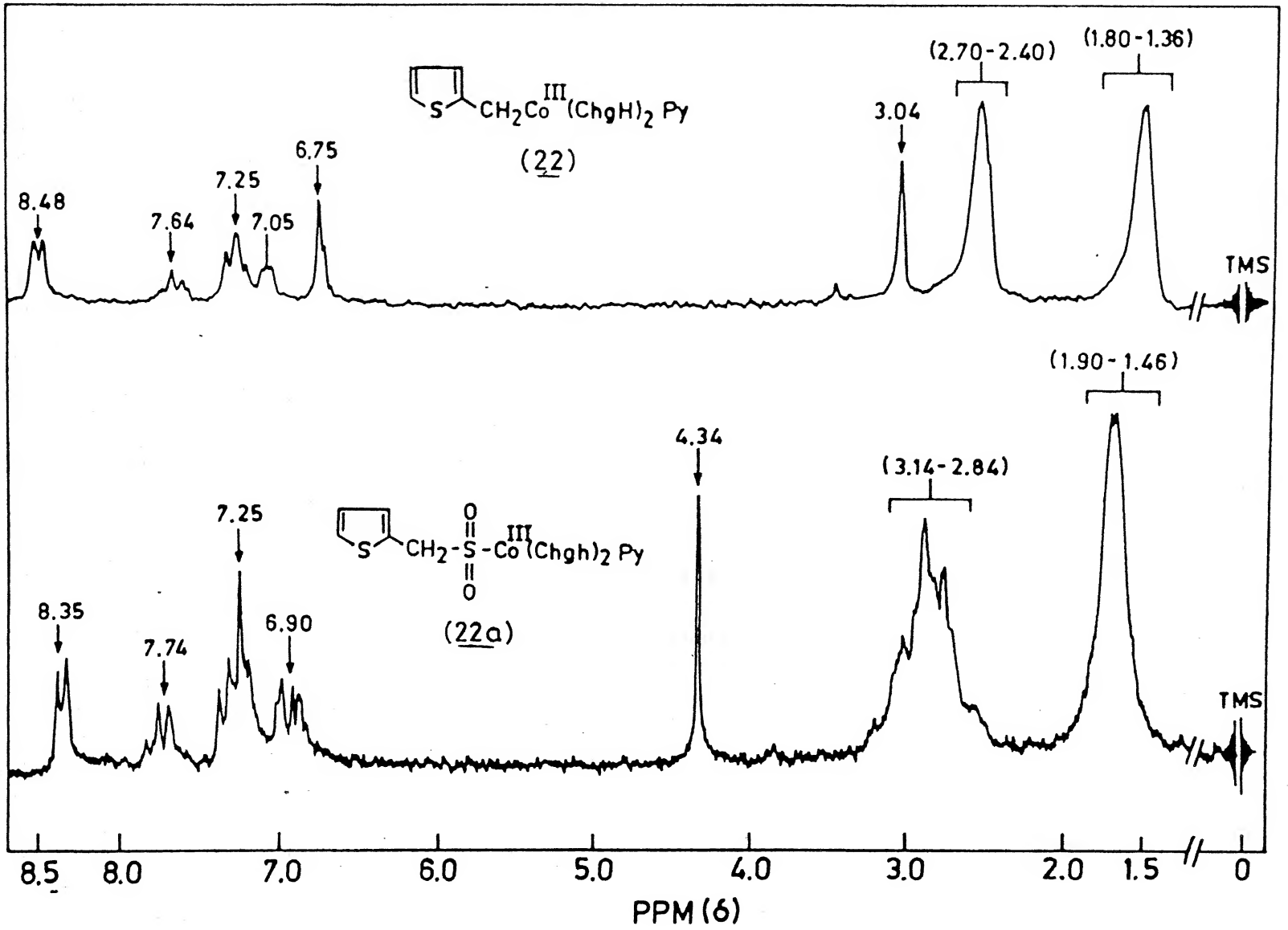
* : Methyl appears at 2.20δ.

Table 3.3: Spectral Characteristics of organo(s-sulphinato)cobaloximes $RCH_2-SO_2-Co^{III}(chgH)_2Py$ (22a-25a)*.

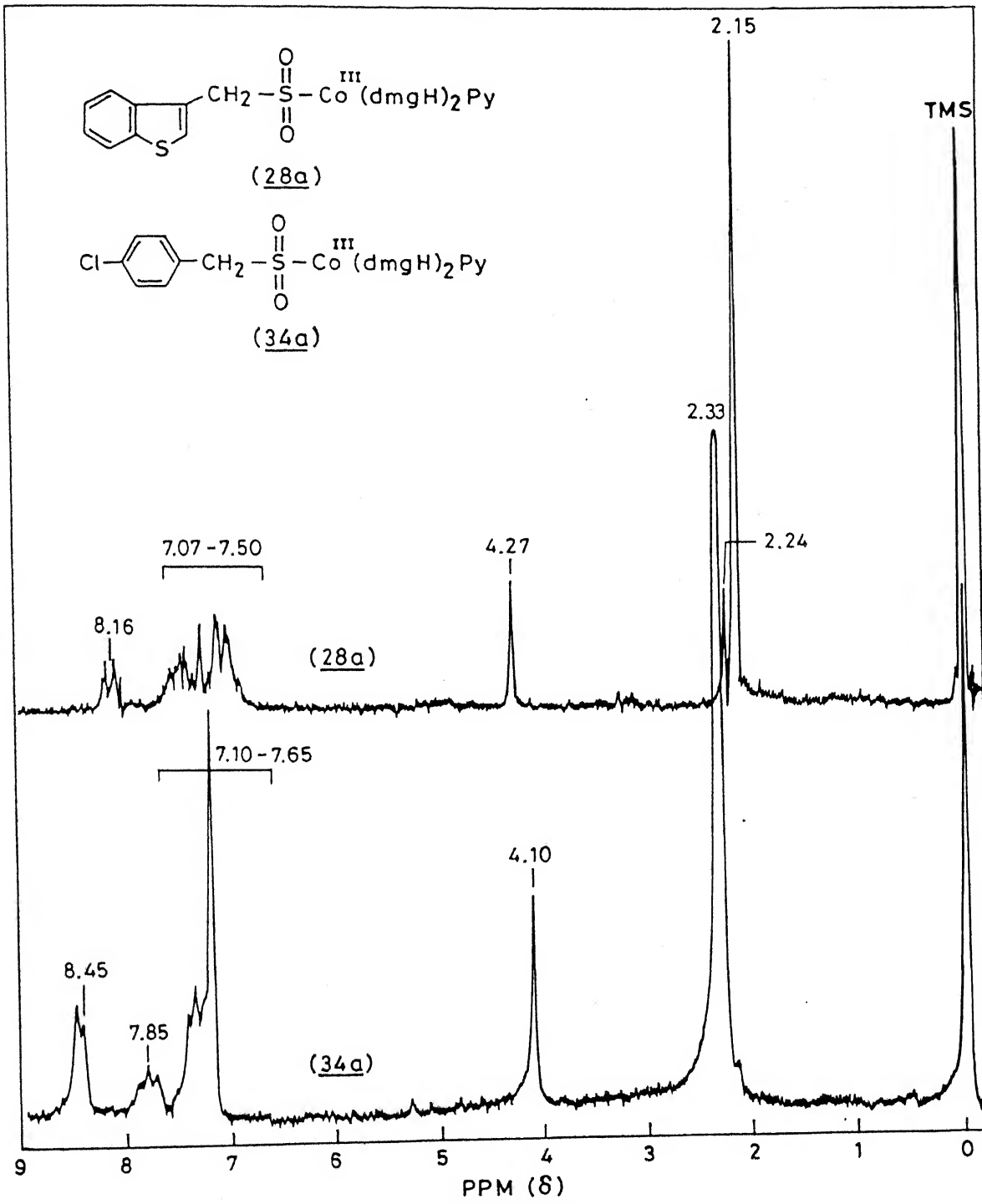
| Compound No. | $RCH_2$ | $^1H$ NMR Chemical shift(δ): $CDCl_3$ | | | | | | $\lambda^{nm}_{(CH_3OH)}$ |
|---|---|---|---|---|---|---|---|---|
| | | Aromatic | $CH_2$ | chgH | Pyridine α | Pyridine β | Pyridine ν | |
| (22a) | 2-Thienylmethyl | 6.90 | 4.34 | 1.46-1.90<br>2.84-3.14 | 7.25 | 7.74 | 8.35 | 347,308,250 |
| (23a) | 3-Thienylmethyl | 7.08-7.50 | 4.18 | 1.20-1.90<br>2.60-3.10 | a | 7.80 | 8.44 | 500,303,248 |
| (24a) | Furfuryl | 6.28 | 4.20 | 1.45-1.92<br>2.64-3.14 | 7.25 | 7.70 | 8.32 | 303,247 |
| (25a) | 3-Furylmethyl | 6.43,<br>7.28-7.71 | 3.98 | 1.43-2.05<br>2.34-3.53 | a | 8.00 | 8.46 | 312,246 |

* For all compounds characteristic IR(KBr) absorption frequencies for ($Co-SO_2$) linkage appear at $\nu_{sym}$ (1060-1070) and $\nu_{asym}$ (1220-1230) $cm^{-1}$.

a: obscured.




$^1$H NMR SPECTRUM (100 MHz) OF (22) AND (22a).




(28a)

(34a)

$^1H$ NMR spectrum (90 MHz) of (28a) and (34a)

3. The reaction is inhibited by galvinoxyl and becomes faster with adventitious cobaloxime(II).

4. No exchange of (14) and (24) into (16) and (22) takes place under the reaction conditions without the presence of sulphur dioxide.

5. Once the inserted products are formed, no rearrangement of any kind is observed. The products are very stable to air.

All the reactions described above are free radical in nature. The radical nature of these reactions is apparent from the observation that the rates of these reactions are variable and subject to induction periods. The cleavage of Co-C bond is a key feature of these substrates and it is well established that the organocobaloximes[308] undergo unimolecular homolysis under thermal and photochemical conditions. This is quite consistent with the low bond energy of Co-C bond which falls between 17-25 kcal/mole in such substrates. Besides, cobaloxime(II) has been shown to be a good leaving group in many known homolytic displacement reactions.[150]

Further indirect support to the radical nature of these reactions comes from the earlier studies of $SO_2$ insertion on hexenyl and butenyl cobaloximes where one of the products obtained is the cyclised product. The product is formed as a result of the ability of the hexenyl radical to undergo cyclisation reactions.[273] Cyclisation without prior dissociation of Co-C bond seems unlikely.

From the nature of products obtained, influence of galvinoxyl and adventitious cobaloxime(II) and based on our work on homolytic displacements at carbon centre in such cobaloximes as described in the 2nd chapter, we propose that the reactions are not true insertionsand the experimental observations can be explained by the following radical chain mechanism.

Scheme 3.5

Initiation:

$$RCH_2Co^{III} \underset{}{\overset{h\nu}{\rightleftharpoons}} R\dot{C}H_2 + Co^{II} \quad \ldots (1)$$

Propagation:

Route A:
$$Co^{II} + SO_2 \longrightarrow Co^{II}SO_2 \quad \ldots (2)$$
$$Co^{II}SO_2 + RCH_2Co^{III} \longrightarrow Co^{III}SO_2CH_2R + Co^{II} \quad \ldots (3)$$

Route B:
$$R\dot{C}H_2 + SO_2 \longrightarrow RCH_2\dot{S}O_2 \quad \ldots (4)$$
$$RCH_2\dot{S}O_2 + RCH_2Co^{III} \longrightarrow RCH_2SO_2Co^{III} + R\dot{C}H_2 \quad \ldots (5)$$

Termination:

$$Co^{II}SO_2 + Co^{II} \longrightarrow Co^{III}SO_2Co^{III} \quad \ldots (6)$$
$$RCH_2\dot{S}O_2 + Co^{II} \longrightarrow RCH_2SO_2Co^{III} \quad \ldots (7)$$

Co = $Co(dmgH)_2Py$ or $Co(ChgH)_2Py$

The concerted mechanism with the attack of sulphurdioxide at the metal and at the organic group is ruled out in view of the experimental observations.

The product $RSO_2Co^{III}$ may arise by two independent routes A and B involving the propagation steps 2,3,4 and 5 respectively. In view of the results described in the 2nd chapter and from our earlier studies, it is well established that the reaction (5) is a key step in many homolytic displacement reactions in organocobaloximes. Therefore, any $R\dot{S}O_2$ radical, formed during the reaction must attack the R group of the organocobaloxime. It is therefore, quite unlikely that $RSO_2Co^{III}$ may arise by route B*. Therefore, the preferred route for the formation of $RSO_2Co^{III}$ must be route A**. There is a good precedent for the reaction (2) from the direct reaction of $SO_2$ with Co(II) complexes, such as $Co(CN)_5^{-3}$ and $Co(dmgH)_2Py$. The former gives the well characterized $[Co(CN)_5]_2SO_2]^{6-}$ supposedly via reaction 2 and 6, but the corresponding complex $(Co(dmgH)_2Py)_2SO_2$ is less well characterized.[173a]

The above mechanism is by no means universal in $SO_2$ insertion reactions but has also been applied to organoiron complexes

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* There is no clear cut example in the literature for the attack of $MSO_2$ radical on the carbon centre.

** Since $PhCH_2SO_2Cl$ reacts with benzylcobaloxime and forms a small amount of the inserted product, $PhCH_2SO_2Co^{III}$, route B therefore, cannot be totally ignored.

under extreme conditions. For example, in the reaction of $SO_2$ with a mixture of (A) and (B), about 5-15% of the inserted cross product $PhCH_2SO_2Co^{III}(dmgH)_2Py$ is also formed implying the attack of $Py(dmgH)_2Co.SO_2$ radical on the organoiron complex.[173a]

$$PhCH_2Fe(Co)_2(\eta\ cp) + 4\text{-}BrC_6H_4CH_2Co^{III}(dmgH)_2Py \xrightarrow{SO_2}$$

(A) (B) $PhCH_2SO_2Co^{III}(dmgH)_2Py$ 5-15%

Interestingly, no crossed insertion products are formed in the reaction of $SO_2$ with a mixture of (A) and organomolybdenum complexes.

In view of Jacobson and Wojcicki's results,[309] it is conceivable that the mechanism of $SO_2$ insertion may differ in liq. $SO_2$ from that in organic solvents, since they have found some changes in the reaction order as a function of R. It is however, very difficult to extend the argument in the present studies since we do not know the precise change in rates in liq. $SO_2$ or in solvent ($CH_2Cl_2$). However, it is worth pointing out that the reaction is much cleaner in liq. $SO_2$ in case of benzyl-cobaloximes where the inserted product is obtained exclusively, whereas the same reaction with $SO_2$ gas gives a side product as mentioned earlier. However, in the benzoanalogues, the products obtained are same with $SO_2$ gas and with liq. $SO_2$.

The implication of the above results very clearly points to the fact that the free radical chain mechanism is dominant in the organocobaloximes. Furthermore, it may introduce in other systems like organoiron, organomolybdenum etc., only when there is a sufficient initiation and when the concentrations are extremely high and the stability of the displaced metal such that the propagation step (3) is favoured.

In view of our results it seems that the lack of reaction of $MeCo^{III}(dmgH)_2Py$ with pure dry sulphur dioxide reported earlier,[310] may have been a result of the absence of radical initiation rather, as proposed earlier, the absence of water.

# RESULTS AND DISCUSSION

## $O_2$ INSERTION

## 3.4 Results

The reaction of oxygen gas with 2-thienylmethyl cobaloximes (14) in $CH_2Cl_2$ at $0^oC$ under irradiation proceeds smoothly and is over within 1 hr (TLC inference only). The corresponding dioxy product (14b) is formed in near quantitative yield. Similarly, the reactions of 3-thienylmethyl, furfuryl, 3-furylmethyl, 2-benzofurylmethyl, 2-thianaphthylmethyl and 3-thianaphthylmethyl bis(dimethylglyoximato)pyridine cobalt(III) complexes (15-20) under identical reaction conditions form the corresponding dioxy adducts (15b-20b) in almost quantitative yield. On the other hand, the reactions of the corresponding cobaloximes having cyclohexaneglyoxime as equatorial ligands (22-28) proceed faster to give the corresponding dioxy products (22b-28b) in quantitative yield. Similar observations are made in the reactions of 2-thienylmethyl bis(dimethyl glyoximato)cobalt(III) complexes (29-31) having different axial bases like γ-picoline, morpholine, and piperidine (Scheme 3.6, Table 3.4, 3.5).

The following observations are made from the overall study

i) the reactions do not proceed in the dark at $0^oC$

ii) the reactions stop as soon as the irradiation is stopped

iii) the rate of reactions is inhibited by galvinoxyl and is accelerated by the addition of $Co^{II}(dmgH)_2Py$ (dimer).

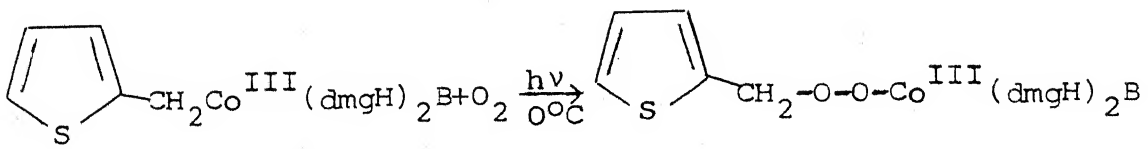
Scheme 3.6

$$RCH_2\text{-}Co^{III}(L_2)Py + O_2 \xrightarrow[0^oC]{h\nu} RCH_2\text{-}O\text{-}O\text{-}Co^{III}(L_2)Py$$

$RCH_2$ =

(14) 2-Thienylmethyl; L = dmgH
(15) 3-Thienylmethyl; L = ''
(16) Furfuryl ; L = ''
(17) 3-Furylmethyl ; L = ''
(18) 2-Benzofuryl-methyl ; L = ''
(19) 2-Thianaphthyl-methyl ; L = ''
(20) 3-Thianaphthyl-methyl ; L = ''
(22) 2-Thienylmethyl; L = chgH
(23) 3-Thienylmethyl; L = ''
(24) Furfuryl ; L = ''
(25) 3-Furylmethyl ; L = ''
(26) 2-Benzofuryl-methyl ; L = ''
(27) 2-Thianaphthyl-methyl ; L = ''
(28) 3-Thianaphthyl-methyl ; L = ''

(14b) 2-Thienylmethyl; L = dmgH
(15b) 3-Thienylmethyl; L = ''
(16b) Furfuryl ; L = ''
(17b) 3-Furylmethyl ; L = ''
(18b) 2-Benzofuryl-methyl ; L = ''
(19b) 2-Thianaphthyl-methyl ; L = ''
(20b) 3-Thianaphthyl-methyl ; L = ''
(22b) 2-Thienylmethyl; L = chgH
(23b) 3-Thienylmethyl; L = ''
(24b) Furfuryl ; L = ''
(25b) 3-Furylmethyl ; L = ''
(26b) 2-Benzofuryl-methyl ; L = ''
(27b) 2-Thianaphthyl-methyl ; L = ''
(28b) 3-Thianaphthyl-methyl ; L = ''




(29b) B = γ Picoline; (30b) B = Morpholine; (31b) B = Piperidine.

Table 3.4: Spectral characteristics of oxygen inserted products, $RCH_2OOCo^{III}(L_2)Py$ (14b-20b) and (22b-28b)

| Compound No. | $^1H$ NMR Chemical shift (δ) $CDCl_3$:TMS | | | | $\lambda^{nm}_{CH_3OH}(\log\varepsilon)$ |
|---|---|---|---|---|---|
| | Aromatic | $CH_2$ | dmgH/chgH | Pyridine α β γ | |
| 1 | 2 | 3 | 4 | 5 | 6 |
| (14b) | 6.80,7.15 | 4.45 | 2.25,2.35 | 7.15,7.60,8.30 | 237(3.28),247(3.42),322(2.92) |
| (15b) | 7.15,7.25 | 4.30 | 2.25,2.35 | 7.10,7.60,8.30 | 231(3.34),244(3.51),312(2.96) |
| (16b) | 6.15,7.15 | 4.25 | 2.30,2.40 | 7.15,7.60,8.30 | 224(3.11),359(2.86),316(2.52) |
| (17b) | 6.30,7.20 | 4.15 | 2.25,2.35 | 7.20,7.60,8.25 | 242(2.98),254(3.20),324(2.61) |
| (18b) | 6.53,7.19,7.33-7.79 | 4.36 | 2.26,2.33 | a a 8.36 | 247(5.18),284(4.86),305(4.71), 545(2.83) |
| (19b) | 7.09,7.21-7.31,7.86 | 4.62 | 2.34,2.44 | a 7.70,8.44 | 230(4.58),245(4.60),253(4.61), 256(4.57),300(4.23),555(2.30) |
| (20b) | 7.16-7.40, 7.64-7.90 | 4.60 | 2.24 | a a 8.42 | 243(4.30),250(4.34),255(4.28), 295(3.90),547(2.15) |
| (22b) | 6.90,7.16 | 4.50 | 1.50-1.90, 2.66-2.84, 2.90-3.06 | 7.24,7.70,8.40 | 250(4.41),313(4.03),553(2.39) |

...contd.

Table 3.4(contd.)

| 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|
| (23b) | 7.02,7.16,7.24 | 4.36 | 1.40-1.82, 2.56-2.80, 2.84-3.00 | 7.24,7.70,8.38 | 249(4.44),305(4.04),558(2.30) |
| (24b) | 6.24,7.26 | 4.32 | 1.36-1.86, 2.64-2.82, 2.88-3.10 | 7.26,7.70,8.38 | 252(4.46),315(4.15),558(2.34) |
| (25b) | 6.29,7.26 | 4.03 | 1.28-1.90, 2.32-3.10 | 7.26,7.70,8.34 | 247(4.40),305(3.98) |
| (26b) | 6.58,7,20,7.38, 7.50 | 4.48 | 1.40-1.90, 2.60-2.84, 2.90-3.20 | 7.24,7.72,8.44 | 247(5.18),284(4.86),305(4.71), 545(2.83) |
| (27b) | 7.32,7.46,7.54, 7.72,7.96 | 4.58 | 1.42-1.82, 2.62-2.84, 2.86-3.14 | 7.28, a 8.36 | 230(4.58),245(4.60),253(4.61), 256(4.57),300(4.23),555(2.30) |
| (28b) | 7.30-7.60 | 4.59 | 1.40-1.86, 2.40, 2.64-3.16 | a ,7.80,8.40 | 213(2.65),245(2.45) |

Table 3.5: Spectral characteristics of organocobaloximes $RCH_2Co^{III}(dmgH)_2B$ (29-31) and their oxygen inserted products $RCH_2OOCo^{III}(dmgH)_2B$ (29b-31b) ($RCH_2$=2-Thienylmethyl)

| Compound No. | $^1H$ NMR Chemical Shift(δ);$CDCl_3$ | | | | $\lambda^{nm}_{CH_3OH}$(log ε) |
|---|---|---|---|---|---|
| | Aromatic | $CH_2$ | dmgH | B | |
| (29)* | 6.63,7.10 | 2.97 | 2.00 | 7.10,8.42 | 375(3.69),280(4.04),238(4.43) |
| (29b)** | 6.89,7.00-7.34 | 4.49 | 2.24,2.34 | a ,8.26 | 568(2.48),303(4.12),249(4.39) |
| (30) | 6.62,7.06 | 2.86 | 2.15 | 2.26-2.78,3.20-3.93 | 375(3.62),280(3.92),235(4.28) |
| (30b) | 7.16,7.63 | 4.73 | 2.43 | 2.16,2.33-2.72<br>3.03-3.85 | 303(4.12),255(4.25) |
| (31) | 6.61,7.09 | 2.93 | 2.06 | 1.03-1.87<br>1.87-2.36 | 379(3.79),285(4.08),238(4.39) |
| (31b) | 6.90,7.22 | 4.39 | 2.49 | 1.06-1.85<br>2.16-3.00 | 558(2.44),283(4.16),245(4.39) |

* Me resonance appears at 2.25 δ

** Me resonance is obscured under dmgH resonance

iv) the reactions become faster as the axial base strength increases (TLC inference only)

v) the best temperature for insertion is found to be $0^{o}C$

vi) when the reactions are carried out in the dark in refluxing dichloromethane no insertion product is formed even after 20 hrs. However after 40 hr , the homolysis of Co–C bond followed by atom abstraction from the solvent lead to the formation of three new cobaloximes in the ratio 6:3:1 which are partially characterised. Two of these products point to as $ClCo^{III}(dmgH)_2Py$ and $CHCl_2Co^{III}(dmgH)_2Py$*. The atom abstraction process is much faster in chloroform solvent ($45^{o}$, 4 hr). One of the major product is identified as $CCl_3Co^{III}(dmgH)_2Py$. NMR($CDCl_3$): δ (2.36)(s), 7.20-8.18(m).

The kinetics of these reactions has been run on a u.v. visible spectrophotometer. The following information is obtained.

Absorbance ($A_t$) is noted down at different intervals and concentration of the product ($C_t$) at any time (t) is calculated as follows.

$$A_t = (Co - C_t)\varepsilon_o + \varepsilon_t C_t$$

$$= \varepsilon_o C_o - C_t\varepsilon_o + \varepsilon_t C_t$$

$$= A_o - C_t(\varepsilon_o - \varepsilon_t)$$

$$\therefore C_t = \frac{A_o - A_t}{\varepsilon_o - \varepsilon_t}$$

---

* NMR($CDCl_3$): δ2.13(s), 5.82(s), 7.3-8.5(m).

$A_t$ = Absorbance at any time (t)

$A_o$ = Initial absorbance

$\varepsilon_o$ = Molar Extinction Coefficient of the initial complex

$\varepsilon_t$ = Molar Extinction Coefficient of the product.

$C_t$ = Concentration of the product at any time (t)

$C_o$ = Concentration of the initial complex

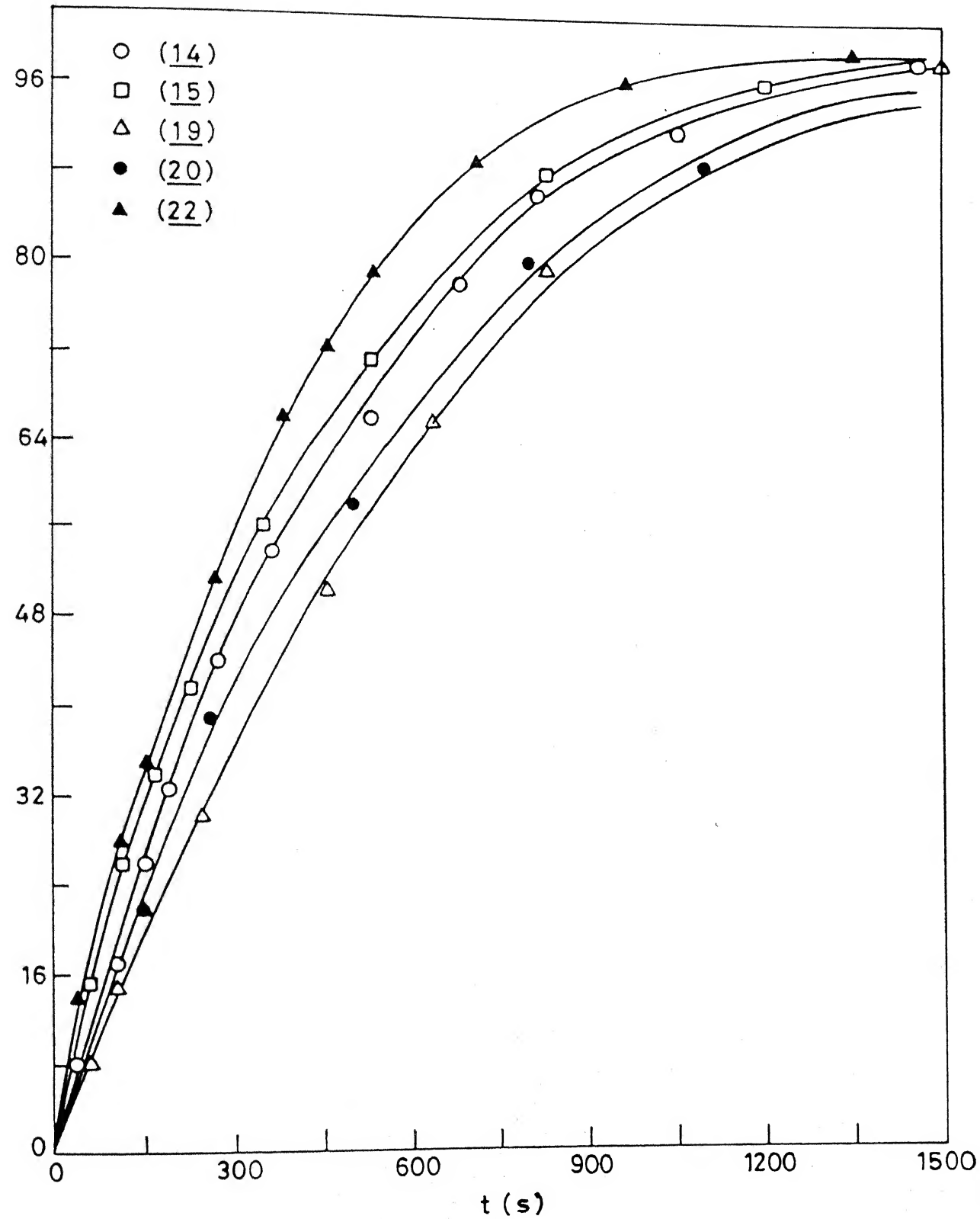
(a) Fig. 1 shows the curves where $C_t$ is plotted against time (t) for the complexes 2 and 3 thienylmethyl cobaloximes (14 and 15), 2 and 3 thianaphthylmethyl cobaloximes (19 and 20) and 2-thienylmethyl bis(cyclohexaneglyoxime)pyridine cobalt(III) (22).

(b) A plot of log $(C_o-C_t)$ vs t gives a straight line (Fig.2) indicating pseudo first order nature of these reactions.

(c) In the experiment (R.6) when $\frac{1}{C_o-C_t}$ vs t is plotted a straight line is obtained which shows that the order of the overall reaction is 2.

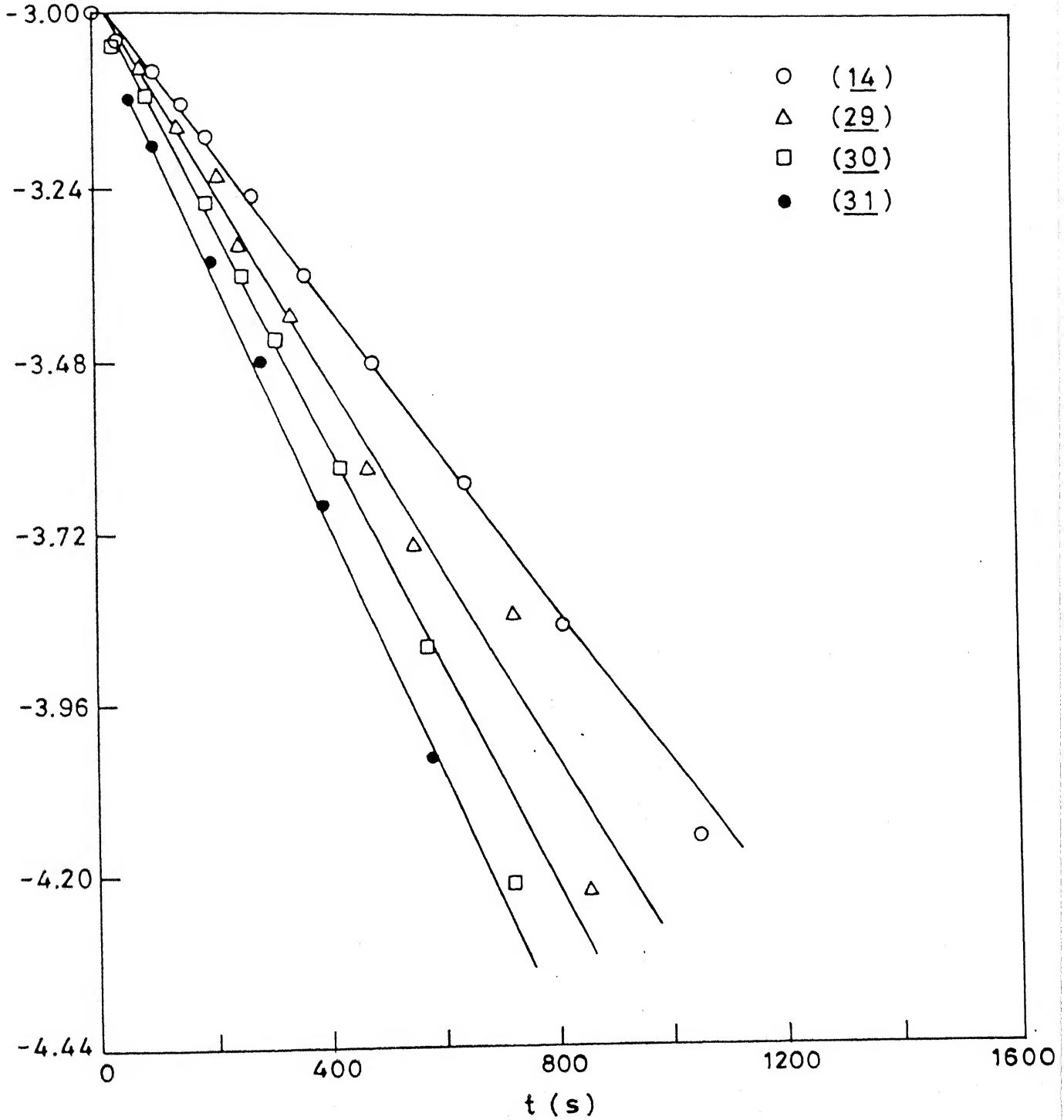
(d) As the axial base ligand strength increases, the rate of the reaction increases in the order Piperidine $>$ Morpholine $>$ $\gamma$ Picolline $>$ Pyridine (Table 3.6).

(e) With the variation in axial R group the differences in the rate of these reactions are less distinct but still perceptible and follow a definite order (Scheme 3.7, Table 3.6).




Plot of $C_t$ (%) versus t

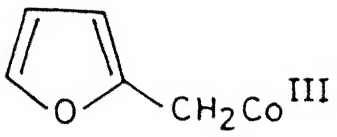
Fig. 1

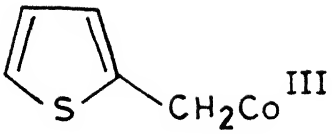



Plot of $\log (C_o - C_t)$ versus t.

Fig. 2

# Scheme 3.7




(16) > 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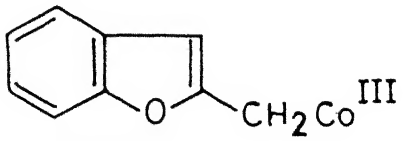
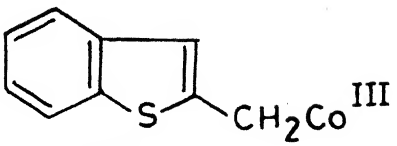



(18) > 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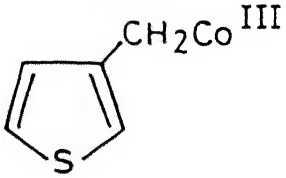
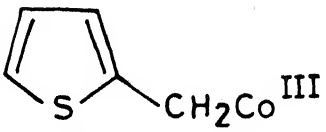



(15) > 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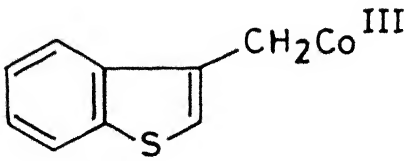
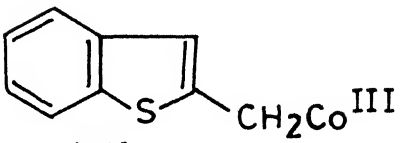
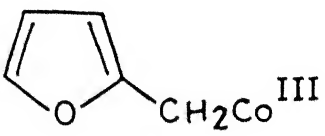
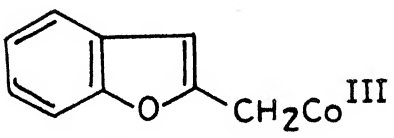


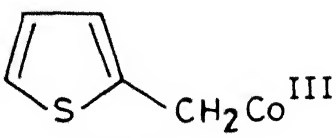

(20) > 

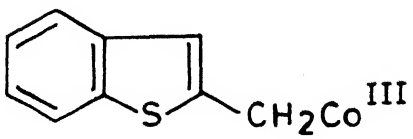

(19)



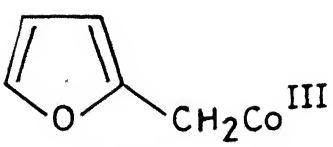

(16) > 

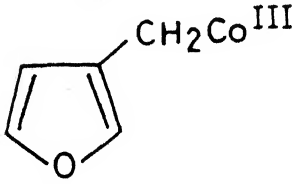

(18)




(14) > 


(19)




(16) > 


(17)

Co = Co(dmgH)$_2$ Py

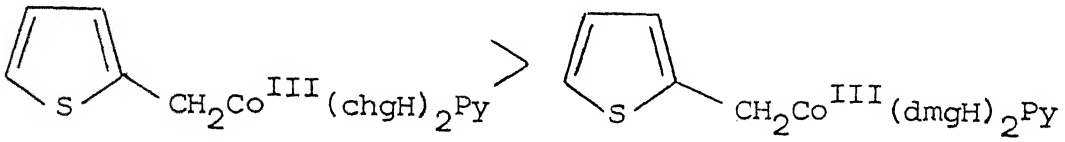
Table 3.6: Rate Constants $(K_{obs})^{*}$ of $O_2$ insertion reaction of Cobaloximes $RCH_2Co^{III}(L_2)B$ [14-20, 22, 24, 29-31]

| Compound No. | $RCH_2$ | L | B | $K_{obs} \times 10^4$, $sec^{-1}$ |
|---|---|---|---|---|
| (14) | 2-Thienylmethyl | dmgH | Py | 25 |
| (15) | 3-Thienylmethyl | '' | '' | 28 |
| (16) | Furfuryl | '' | '' | 26 |
| (17) | 3-Furylmethyl | '' | '' | 22 |
| (18) | 2-Benzofurylmethyl | '' | '' | 23 |
| (19) | 2-Thianaphthylmethyl | '' | '' | 15 |
| (20) | 3-Thianaphthylmethyl | '' | '' | 16 |
| (22) | 2-Thienylmethyl | chgH | '' | 30.6 |
| (24) | Furfuryl | '' | '' | 31.7 |
| (29) | 2-Thienylmethyl | dmgH | γ-Picoline | 30.6 |
| (30) | 2-Thienylmethyl | '' | Morpholine | 35 |
| (31) | 2-Thienylmethyl | '' | Piperidine | 40 |

*Rate $= K[RCH_2Co^{III}(L_2)B][O_2]$

$= K_{obs}[RCH_2Co^{III}(L_2)B]$

(f) Heteroaromatic methyl cobaloximes having cyclohexane glyoxime as equatorial ligands undergo $O_2$ insertion readily than the corresponding cobaloximes containing dimethylglyoxime as equatorial ligands (Table 3.6) i.e.




X = S (22) X = S (14)

X = O (24) X = O (16)

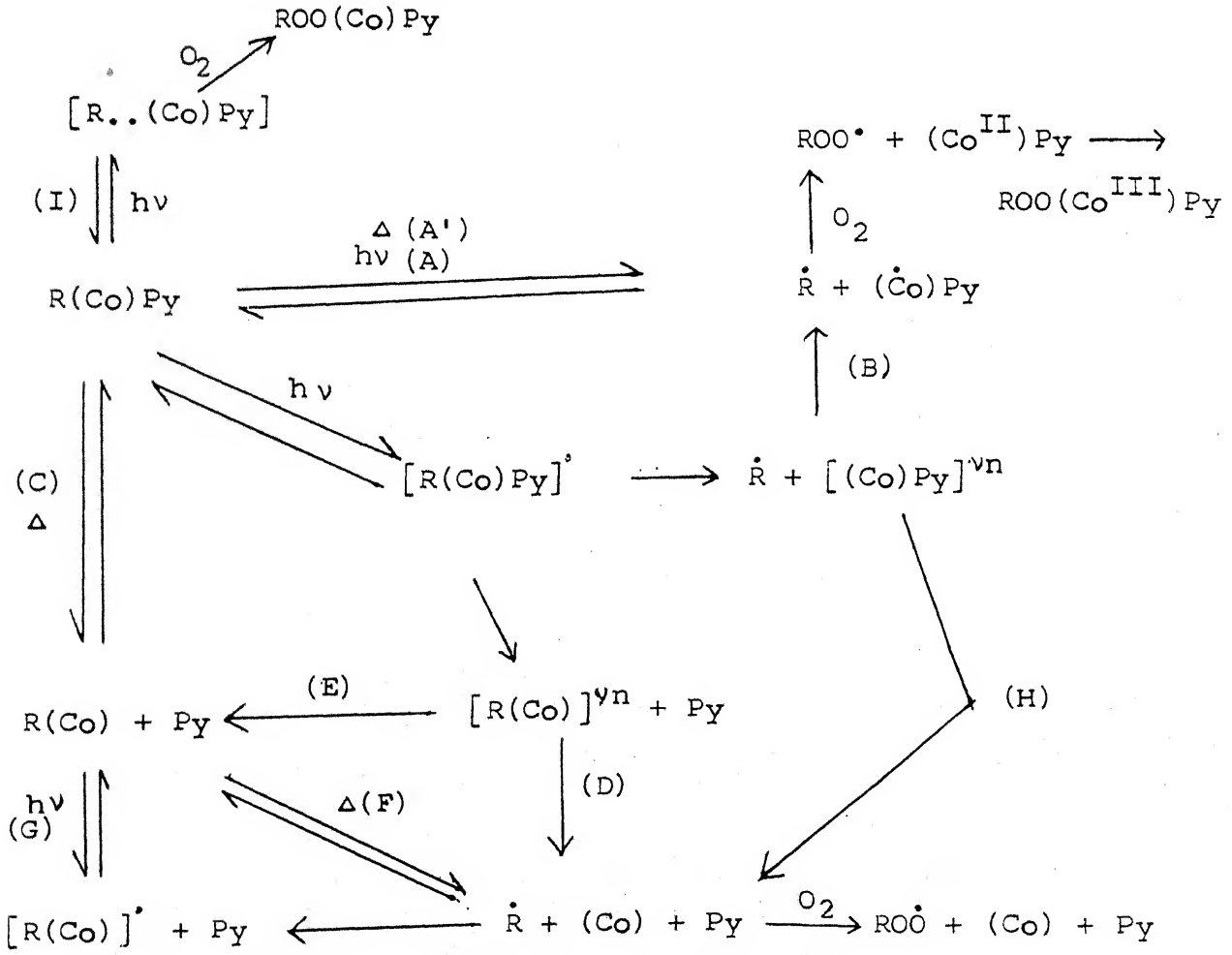
## Discussion

Oxygen insertion into C-M bond is a reaction which takes place with a remarkably wide range of organometallic compounds.[308b,311-316] Both thermal and photochemical activation of these insertions have been observed in the Co-C bond of organocobalt complexes.[184] Conflicting suggestions have been made by various workers, for example, Schrauzer has proposed, based in part on molecular orbital calculations, that photolysis of alkylcobaloximes leads to excitation and subsequent homolytic cleavage of the Co-C bond.[106] Giannotti and coworkers have suggested that photolysis with light in the charge transfer region (about 450 nm) leads to the expulsion of axial base ligand as the primary photochemical

process.[280] The Co–B bond is reformed after the insertion has taken place. The kinetic studies[184,280] have been conducted on the insertion of $O_2$ into R Co(dmgH)$_2$B. For thermal insertions, the reaction rate increases in the order R = $Me_2CH << PhCH_2 < R^1R^2CH=CHCH_2 <$ PhCHR whereas for photochemical reactions, the rates increase in the order R = Me< alkyl < allenyl < propargyl < benzyl < allyl. However, for both, first order dependence on the cobalt complex and on $O_2$ has been observed.[184]

Several mechanisms can be envisaged for the insertion of oxygen into Co–C bond in organocobaloximes (Scheme 3.8).

Scheme 3.8



In addition to all these mechanisms, a radical chain mechanism can also be envisaged.

Initiation:

$$R(Co^{III})Py \longrightarrow R^{\bullet} + (Co^{II})Py$$

Propagation:

$$R^{\bullet} + O_2 \longrightarrow ROO^{\bullet}$$

$$ROO^{\bullet} + R(Co^{III})Py \longrightarrow ROO(Co^{III})Py + R^{\bullet}$$

Termination:

$$R^{\bullet} + R^{\bullet} \longrightarrow R\text{-}R$$

$$R^{\bullet} + ROO^{\bullet} \longrightarrow ROOR$$

If this mechanism is operative, the following characteristics should have been observed.

(a) Necessity of an initiation reaction for the formation of radicals. This initiation reaction may be the rupture of Co-C bond yielding a cobalt(II) complex and the $R^{\bullet}$ radical.

(b) Free radical chain reactions are generally accompained by an induction period.

(c) Once the reaction starts, it proceeds to completion even after the external stimulation (thermal or photochemical) is removed.

In view of our experimental observations that i) there is no induction period, ii) reaction stops as soon as the light stimulation is cut off and iii) the organocobaloximes in the absence of oxygen, are stable at 30°C, i.e. at a temperature where the kinetics indicates that the insertion takes place readily. We therefore rule out the participation of such a free radical chain mechanism in the present study.

Among the mechanisms given in (Scheme 3.8) some can be easily eliminated on the basis of the simple experimental observations made in these reactions, for example, since no insertion has been observed in the dark under thermal conditions, all mechanisms involving thermal conditions are not considered. Similarly any photochemical process where loss of pyridine is observed can be eliminated because if such a base off process is occuring, the rate of insertion should have increased with the decrease in base strength. However,a reverse order has been observed i.e. the rate of insertion is found to increase as the base strength increases. So only three mechanisms (A, B and I) remain as possibilities. It seems difficult to distinguish between these mechanisms without doing a more detailed study on these complexes. However, the following plausible rational is given.

The basic difference between mechanisms A, B and I is that in the former case, the direct free radicals $R^{\bullet}$ and CoPy

are involved. $R^{\bullet}$ picks up $O_2$ and finally combines with (Co)Py to give the inserted product. The stability of the organo free radical species should therefore play an important role and the rate of insertion should accordingly be effected in such a case. On the other hand mechanism I, does not invoke a complete rupture of Co–C bond, however the resulting ($R^{\bullet}$....Co) radical is in the solvent cage, which on reaction with $O_2$ gives the final inserted product.

We prefer mechanism I in view of the following facts i) the rates of insertion vary much less with the change in R group which may suggest that the complete rupture of Co–C bond may not be the slow step in the photochemical reaction ii) the rate law corresponding to this mechanism is

$$\text{Rate} = \frac{K_1 K_2 [RCo(dmgH)_2B][O_2]}{K_{-1} + K_2[O_2]}$$

Where $R\text{-}Co^{III} \underset{K_{-1}}{\overset{K_1}{\rightleftharpoons}} [R^{\bullet}....Co]$

$$[R^{\bullet}...Co] + O_2 \xrightarrow{K_2} ROOCo^{III}$$

Assuming $K_{-1} \gg K_2[O_2]$, the rate law becomes

$$\text{Rate} = K_{exp.}[RCo(dmgH)_2B][O_2]$$

Thus the reaction is first order with respect to both the complex and oxygen. This is what is observed in the present studies.

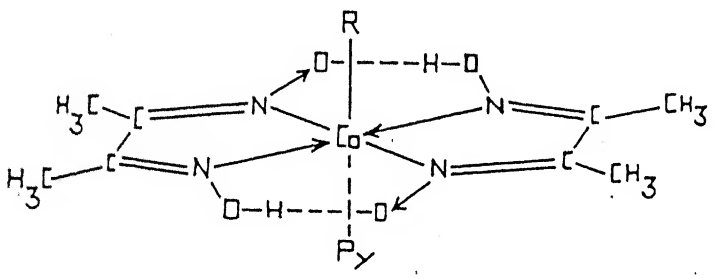
iii) A similar observation has been made by Gaudemer and Charreton.[184]

Although we believe that this mechanism is most likely in the present studies, however it is very difficult to differentiate this mechanism from the fully concerted mechanism where the rupture of Co–C bond would take place simultaneously with the formation of Co–O and O–R bonds. Moreover we also agree with Gaudemer et al.[184] that the results of the kinetic study of the insertion of oxygen in presence of visible light are very difficult to interpret owing to the greater complexities of these reactions. The exact role of light in these reaction is difficult to predict.

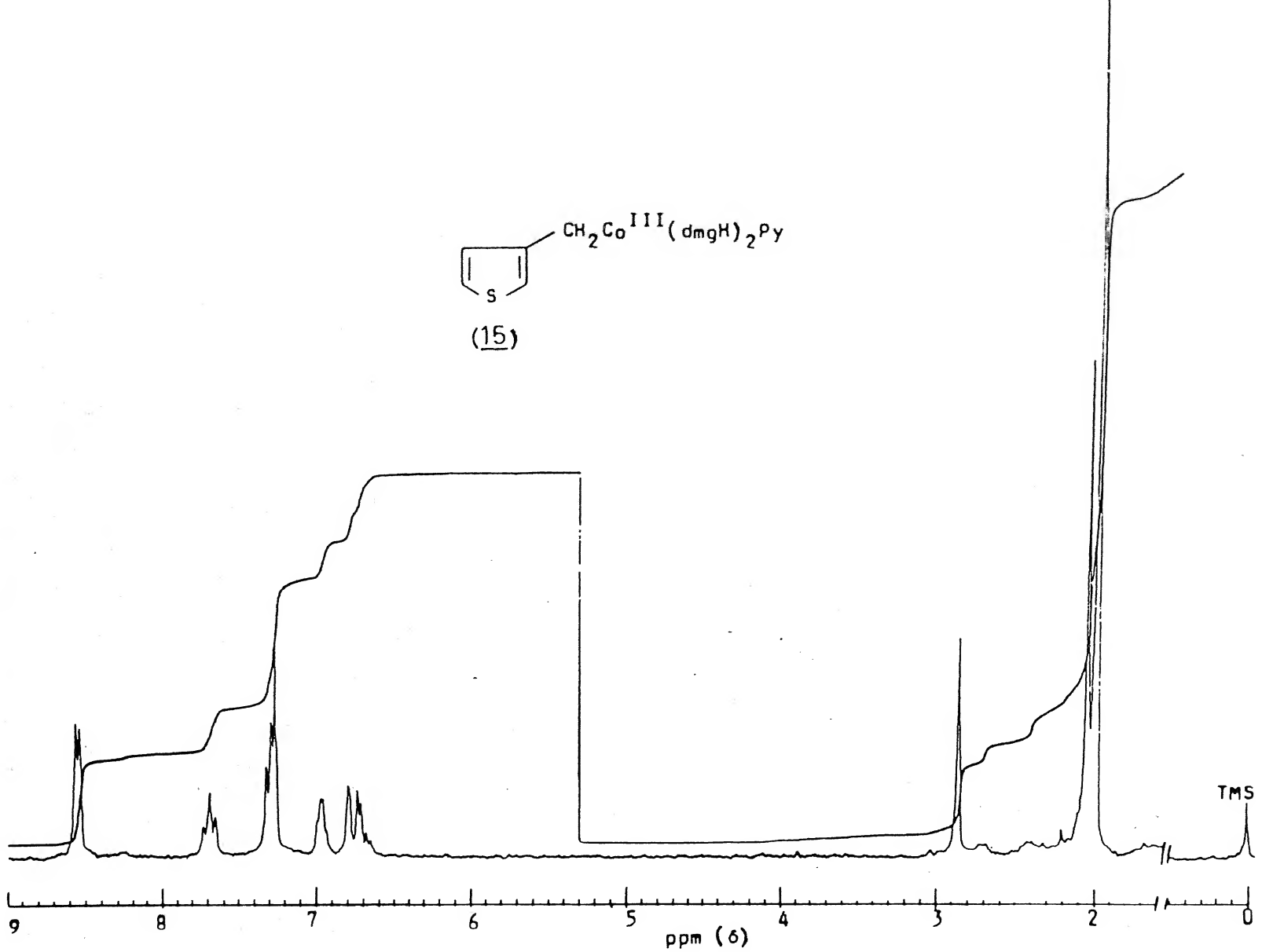
## 3.5 $^{1}$H NMR spectra of cobaloximes (14–20), (14a–20a) and (14b–20b): Unexpected Non-equivalence of Methyl groups

The cobalt atom is nearly coplanar with the four nitrogens of the dimethylglyoxime in the organocobaloximes having less bulky axial ligands. However, the deviation from coplanarity occurs and is dependent upon the steric as well as electronic factors of the axial ligands.[101] For example, if one axial ligand is bulky, the cobalt atom is displaced from the equatorial plane towards the bulky ligand and if both are bulky, the four nitrogens become distorted from planarity. In addition, the

dimethylglyoxime monoanions, while rigid themselves, may not be exactly coplanar but may lie at an angle to each other although the folding is small except for very bulky ligands. Despite this deviation from coplanarity, the $^1$H NMR spectra of organocobaloximes is very simple, the dimethylglyoxime methyl groups appear as singlet at around 2.0–2.4 δ in most cases indicating that such distortion is not sufficient enough to cause non-equivalence of the four equatorial methyl groups.

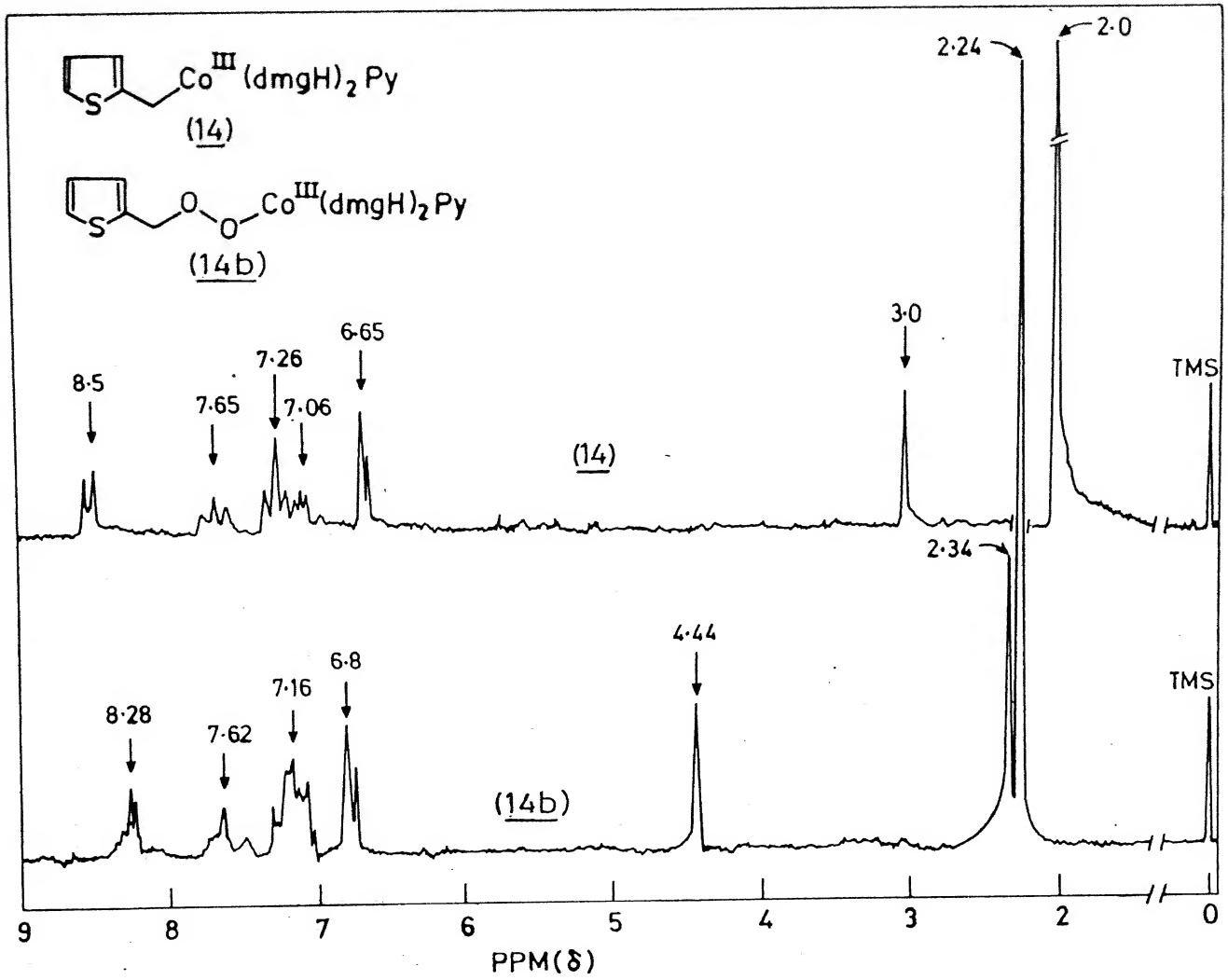


Interestingly we have observed that the organocobaloximes and their inserted products in the present study show an unexpected non-equivalence of the four methyl groups in the $^1$H NMR spectra. The two signals appear in the ratio of 3:1 at about 0.1 ppm apart (table 3.7). In some cases we the 60 and 90 MHz spectra are not well resolved and the methyl groups appear as

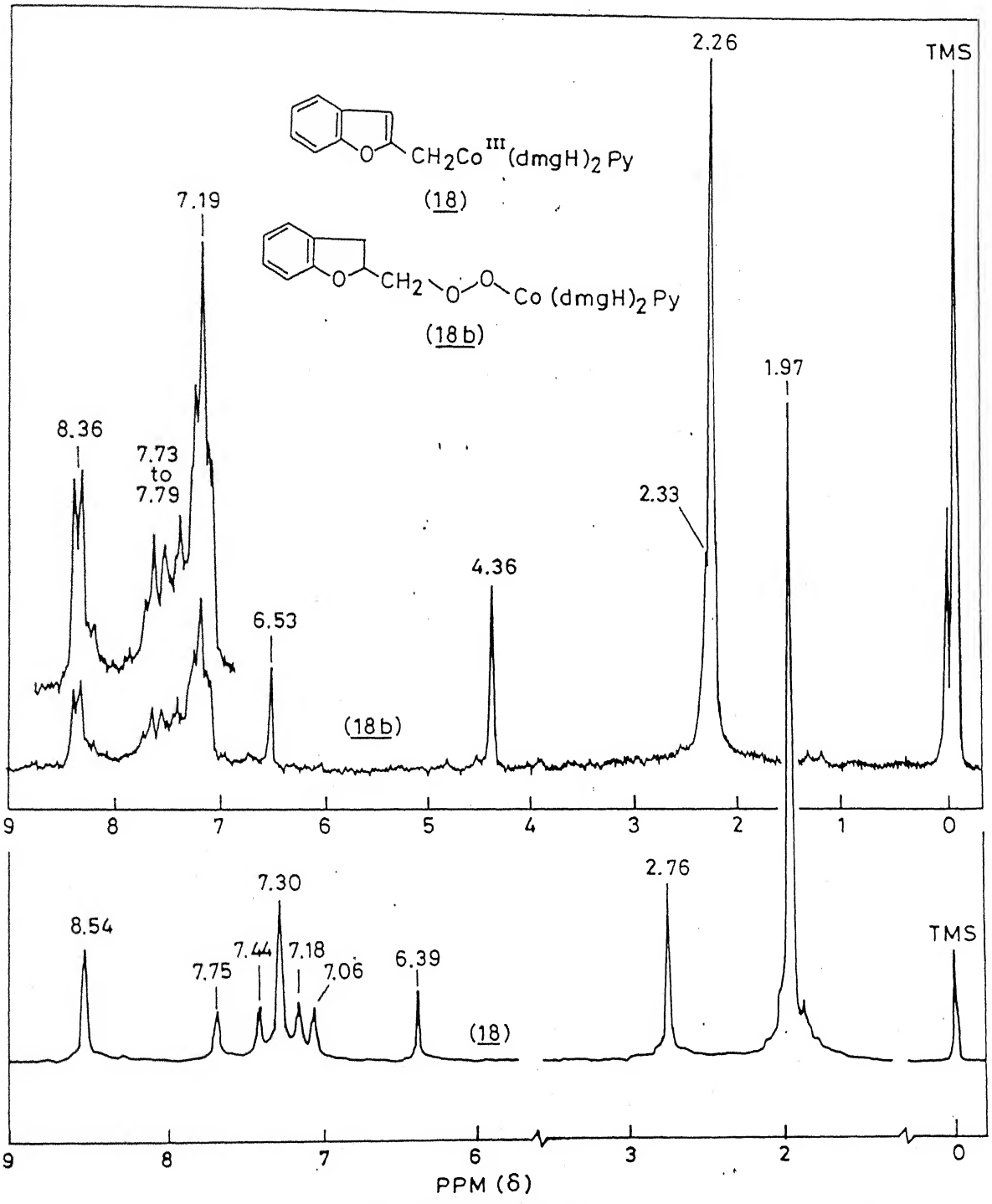



(15)

$^1$H NMR SPECTRUM (200 MHz) OF (15)




$^1H$ NMR SPECTRUM (90 MHz) OF (14) and (14b)




$^1$H NMR SPECTRUM OF (18) (400 MHz) AND (18b) (90 MHz)

Table 3.7: $^1$H NMR Chemical shift[a] (δ); 'dmgH' proton of $RCH_2Co^{III}(dmgH)_2Py$ (14-20), $RCH_2SO_2Co^{III}(dmgH)Py$ (14a-20a) $RCH_2OOCo^{III}(dmgH)_2Py$ (14b-20b)

| $RCH_2$ | $RCH_2Co^{III}(dmgH)_2Py$ | | $RCH_2SO_2Co^{III}(dmgH)_2Py$ | | $RCH_2OOCo^{III}(dmgH)_2Py$ | |
|---|---|---|---|---|---|---|
| | Compound No. | dmgH | Compound No. | dmgH | Compound No. | dmgH |
| 2-Thienylmethyl | (14) | 2.05 | (14a) | 2.25<br>2.38 | (14b) | 2.25<br>2.35 |
| 3-Thienylmethyl | (15) | 2.00<br>2.10 | (15a) | 2.25<br>2.40 | (15b) | 2.25<br>2.35 |
| Furfuryl | (16) | 2.00 | (16a) | 2.30<br>2.40 | (16b) | 2.30<br>2.40 |
| 3-Furylmethyl | (17) | 2.00<br>2.10 | (17a) | 2.25<br>2.38 | (17b) | 2.25<br>2.35 |
| 2-Benzofurylmethyl | (18) | 1.97 | (18a) | 2.26 | (18b) | 2.26<br>2.33 |
| 2-Thianaphthylmethyl | (19) | 2.00 | (19a) | 2.40<br>2.56 | (19b) | 2.34<br>2.44 |
| 3-Thianaphthylmethyl | (20) | 1.85<br>1.95 | (20a) | 2.15<br>2.24 | (20b) | 2.24 |

a, These values also appear in Tables 3.1, 3.2 and 3.4.

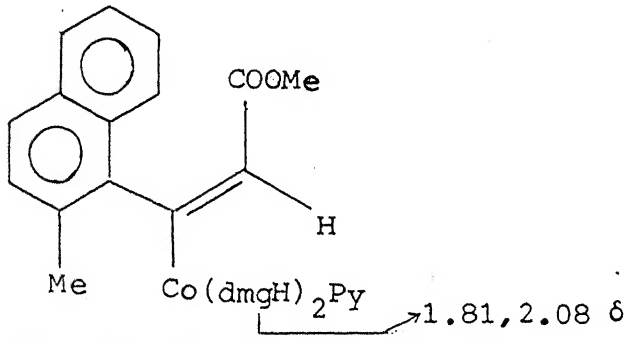
broad singlet at 2.0 δ. However, the non-equivalence (3:1) is clearly visible for these systems in 200 and 400 MHz spectra.

Though this kind of non-equivalence is observed for the first time in organocobaloxime chemistry, however the phenomenon of non-equivalence is not unprecedented in literature. It was first pointed out by Gaudemer et al. who speculated that the presence of an asymmetric centre on the axial sigma bonded ligand leads to the non equivalence.[53] They found that the spectra of a number of complexes with $Co-CR^1R^2R^3$ moities show this feature which is also formed in cobaloximes with symmetrical axial alkyl groups (e.g. methyl), having axial bases with an asymmetric carbon centre as in $C_6H_5CH(NH_2)COOMe$ or a donor atom which once bound, becomes asymmetric[297] i.e. $PhCH_2NHCH_3$

| | dmgH(δ) |
|---|---|
| $MeCH(CN)-Co^{III}(dmgH)_2Py$ | 2.19, 2.22 |
| $CH_3Co^{III}(dmgH)_2NH(CH_3)CH_2Ph$ | 2.28, 2.30 |
| $C_6H_5CH(Me)Co^{III}(dmgH)_2Py$ | 2.00, 2.06 |
| $C_6H_5CH(Me)-O-O-Co^{III}(dmgH)_2Py$ | 2.14, 2.23 |

Recently the same workers have observed two signals in the $^1H$ NMR spectra, corresponding to six protons each, for the diastereotopic methyl groups of the dioximato moiety in atropisomeric alkenyl cobaloxime.[98] However, the difference in chemical

shifts of the equatorial methyl groups is large in these systems. This arises because of the close proximity of the equatorial methyl groups to the naphthyl group which lies approximately parallel to the plane of the equatorial ligand.




Recently the same observation is made by Brown et al.[56] A similar explanation was offered earlier for the same observation in the $^1$H NMR spectra of trans (3,3,4,4-tetracyano-2-phenylcyclopentyl)-cobaloximes by Johnson et al.[92]

It seems well established from all the cases known in the literature that the asymmetry in the axial organic or axial base ligand leads to two diastereotopic pairs of methyl groups which result in the presence of two different methyl resonances in the $^1$H NMR spectra.

Interestingly it has been observed that the chirality at the cobalt centre due to the equatorial ligands does not lead to such non equivalence.[97] Recently, cobaloximes of the type $R_2NC(O)SCH(Me)Co^{III}(dmgH)_2Py$, synthesised by Simandi et al.,[65] show such a non equivalence of equatorial methyl group (2.12,2.16δ).

The phenomenon of non equivalence observed in the present study is a novel observation and these systems present the first example of its kind where one of the four methyl groups is placed in a different enviournment. Looking into the literature work, it seems that alkyl, benzyl, allyl, propargyl, allenyl, butenyl, hexenyl, cyclopentylmethyl, cyclohexyl etc. cobaloximes and their dioxy adducts do not show such non equivalence of dimethylglyoxime ligand.[173,190,317-319] Therefore, the phenomenon observed in the present studies must be associated with the presence of heteroatom in the axial organic group. The molecular model of furfuryl dioxy cobaloxime shows that the heteroatom lies directly above the oxime hydrogen (see fig. 3 ). Therefore the main reason might be the new hydrogen bond interaction between the oxime hydrogen and the heteroatom of the axial organic group, which will restrict the free rotation of Co–X (X = C, S or O) bond and result in the observed 3:1 non equivalence. Since it has been observed that tetrahydrofurfuryl cobaloxime

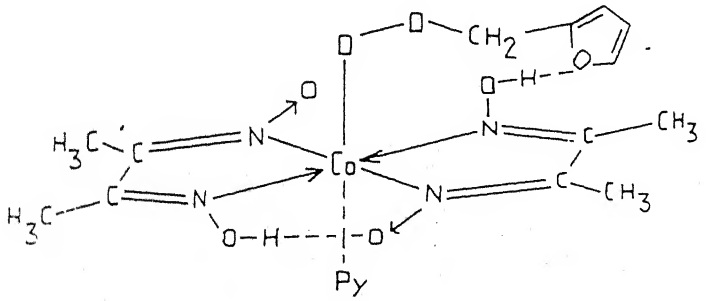



Fig.3

and its dioxy adduct do not show such a phenomenon[232,233] it may point to the necessity of aromatic heteroatom for such a process. However, this cannot be taken as a necessary requirement in view of our similar observation in the organocobaloxime of the kind $PhXCH_2Co^{III}(dmgH)_2Py$ (X = O,S) and their dioxy adducts.[320]

The conclusive evidence in support to the above observation can be made if the $^1H$ NMR spectral studies in different solvents is done and if the new hydrogen bond formation is the main cause, then the $^1H$ NMR study of the $BF_2$ bridged complexes, $RCo(dmgBF_2)_2Py$ (R = thienylmethyl, furylmethyl) is crucial since the hydrogen bond is absent in such systems.

We have not been able to carry out the above studies because of many constraints. However, we are seeking help from Prof. K.L. Brown, Univ. of Texas at Arlington and hope to come up with suitable explanation.

## CONCLUSION AND SCOPE FOR FUTURE WORK

The study of organocobalt(III) complexes has occupied an unusual position linking together organometallic chemistry, co-ordination chemistry and biochemistry. Tremendous amount of work has already been done on these complexes, primarily with an aim to understand the chemistry and the mechanism of the $B_{12}$ coenzyme catalysed reactions which have no parallel in the organic and organometallic chemistry. However, the chemistry of organocobaloxime complexes is so fascinating that it has projected itself in the recent past as more of an independent area rather than as model for the coenzyme $B_{12}$. These complexes offer interesting challenges to the preparative organometallic chemists to apply new reagents and reactions of these complexes. The work in the foregoing chapters has highlighted the organometallic aspects of the organocobaloximes.

Bimolecular homolytic displacement reactions at saturated carbon centre, the $S_H2$ reactions, which were initially thought to be highly improbable reactions and have usually been discarded in literature[150] are successfully studied in this thesis. The synthesis of benzyl and heteroaromatic methyl aryl sulphones has been achieved in reasonably good yield. The present method utilises an efficient synthesis starting from the inexpensive alcohol or halide

$$RX \xrightarrow{(Co)^{I}} R(Co)^{III} \xrightarrow{R'SO_2Cl} RSO_2R' + Cl(Co)^{III}$$

R = benzyl or heteroaromatic methyl,

X = halide

On the basis of experimental evidences we have proposed that these products arise by an exclusive attack of the organosulphonyl radical, $R'SO_2$, at the α carbon centre of the organocobaloximes and these reactions form part of a chain process. However, the mechanism of these reactions demands further study.

Though it is well established from the product distribution, stereochemical, kinetic and thermodynamic studies that the displacement of one paramagnetic metal complex by another identical or near identical metal complex proceeds solely via a concerted homolytic displacement reaction,[150] similar reaction with a greatly dissimilar radical like $R'\dot{S}O_2$, may take place by a two stage process in which an electron transfer is followed by a heterolytic displacement.

$$R'\dot{S}O_2 + R(Co)^{III} \longrightarrow R'SO_2^- + R(Co)^{IV} \xrightarrow[\text{or } S_N2]{S_N1} R'SO_2R + (Co)^{II}$$

Since one electron oxidation of organocobalt(III) species by organosulphonyl radicals is not known in literature, the validity of the label $S_H2$ will still remain in doubt until more studies are done on these systems. Recent work by Espenson et al.

is noteworthy.[262g] They have pointed out from their kinetic studies on the alkyl and benzyl cobaloximes with aliphatic free radicals that the label $S_H2$ or $S_H2'$ is still not proven. They have proposed that the results are best explained by addition-elimination mechanism where radical addition takes place at the nitrogen end of C=N bond of the macrocycle cis to Co-C bond followed by reductive elimination. However, benzyl cobaloximes do not follow this mechanism.

More study which will widen the scope of this reaction need to be investigated, for example, most of the study so far has confined to carbon or sulphur centered radicals only. Other organic radicals/radical cations, particularly heteroatom centered, which are able to manifest such transformations are worthy of investigation. Recent studies with $RSO_2\dot{N}Me$ and $\dot{S}CN$ etc. have resulted in a dichotomy in the free radical vs nucleophilic displacement mechanism.[174b,320] Preliminary study with chlorosulphonyl isocyanate and N,N-dichlorourethane have met with little success.[321] While organocobaloximes are useful substrates, the equatorial dimethylglyoximo ligands themselves are a little too succeptible to attack by radical reagents. It would be useful to survey the influence of different, especially inert, equatorial ligands on the character of the displacement reactions.

Bimolecular homolytic displacements at carbon are by no means confined to organocobaloxime alone. The formation of

4,4,4-trichlorobutene was noted by Kharasch in 1949, in the reaction of allyl bromide with $CCl_4$ and several similar processes have subsequently been detected as components of more complicated systems.[322] More recently, the displacement of the tributyltin radicals from tributylallyltin compounds by trihalomethyl,[323] acyl[324] and phenyl radicals[325] has been described, as well as the displacement of thiyl and arenesulphonyl radicals by tributyltin radicals during the reduction of allyl sulphides and allyl sulphones, but not sulphoxides, with tributyltin hydrides[326] (eqn. 1 and 2).

$$CH_2{=}CH{-}CH_2X + \dot{Y} \longrightarrow YCH_2{-}CH{=}CH_2 + \dot{X} \quad \ldots (1)$$

$\dot{Y}$ = Ph, RS, $CCl_3$, $\dot{X}$ = Br, $Bu_3Sn$, RS

$$Bu_3\dot{S}n + CH_2{=}CH{-}CHRSO_2Ar \longrightarrow Bu_3SnCH_2{-}CH{=}CHR + \dot{S}O_2Ar \quad \ldots (2)$$

Recently, organochromium complexes have been studied as possible substrates for such a process.[327]

The close similarity between these free radical reactions of cobalt, tin, chromium etc., suggests that the general phenomenon of homolytic displacement of metals may be much more common than has previously been supposed. It is particularly likely to be found in transition metal chemistry under conditions where the substrate (A) is co-ordinatively saturated, where the n additional ligands L are such as to reduce the redox potential between $M^m$ and

$M^{m-1}$ (where m and m-1 are the oxidation states) and where the organic group R is accessible to attack by the radical. For the chain reaction to operate, there is additional condition that the displaced metal complex must be sufficiently reactive to regenerate the appropriate organic radical X from XY. A delicate balance between stability and reactivity of the intermediate metal complex $M^{m-1}Ln$ is thus an essential feature for such a process

$$\underset{(A)}{RM^{m}Ln} + \dot{X} \longrightarrow RX + M^{m-1}Ln$$

$$M^{m-1}Ln + XY \longrightarrow YM^{m}Ln + \dot{X}$$

Lastly, organocobaloximes have shown a remarkable ability to initiate many organic transformations resulting in the C-C bond formation.[39,128b,213,262c,328] More work in this direction will be quite useful.

In the molecular insertion study, sulphur dioxide has been shown to insert readily into the Co-C bond in organocobaloximes. The results demonstrate that insertion is the name for an overall process, not for a mechanism. An unambiguous experimental proof in support of the radical chain mechanism has been presented, thus casting a doubt on the true insertion nature of these reactions. One of the steps proposed in the reaction scheme is the attack of $Co^{II}SO_2$ on the carbon centre of the organo-cobaloxime displacing cobaloxime(II). Since no clear cut

examples are known in the literature about such reactions, more work is needed to confirm the validity of attack of $MSO_2$ species on the carbon centre in organocobaloximes. A detailed kinetic study to reach an unambiguous mechanism for such reactions will be quite useful.

Oxygen insertions, on the other hand, are found to be non chain free radical reactions and exclusively form 1:1 dioxy products. A detailed kinetic study on these reactions point to a radical cage mechanism. Since the exact role of light in these reactions is very difficult to predict, a much more systematic and detailed kinetic study is required. There is very little work done on the stereochemical study of these reactions and all reports point to the nonstereospecific nature of these reactions. More work in this direction would be quite useful. The homolysis of Co-C bond accompained by atom abstraction from the solvent molecules to form new Co-H and Co-C bond is of particular relevance to the mechanism of $B_{12}$ dependent dehydrase. Very little attention has been made in this direction.[190]

Following the recent reports that the oxygen inserted organometallic complexes are capable of catalysing many important industrial chemical transformations,[192,299] a new and wide scope for these complexes is anticipated.

The above discussion may pursuade due to think that the organocobaloximes have a great potential in mediating both organic and inorganic transformations. However, its ability to act as model for vitamin $B_{12}$ coenzyme cannot be overlooked.

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